Int. j. adv. multidisc. res. stud. 2024; 4(6):624-627

Received: 10-10-2024
Accepted: 20-11-2024

International Journal of Advanced Multidisciplinary Research and Studies

ISSN: 2583-049X

Antibiotic Resistance in humans due to Microbes

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DOI: https://doi.org/10.62225/2583049X.2024.4.6.3485
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Abstract

Background

Antibiotics are now facing a crisis of resistance. Overuse and misuse have led to bacteria developing resistance, making infections harder to treat. This is exacerbated by the availability of antibiotics without prescriptions and their presence in the environment. The spread of resistant bacteria poses a significant threat to global health, requiring urgent action. Governments and international organizations are working to combat this issue, but the problem persists. Addressing antibiotic resistance requires responsible use and the development of new antibiotics.

Objective

This study aimed to review antibiotic resistance in humans due to microbes.

Discussion

Antimicrobial resistance (AMR) is a natural process where microorganisms stop responding to antibiotics, making infections harder to treat and increasing the risk of spreading serious diseases. The overuse of antibiotics accelerates this process, promoting AMR spread through distinct mechanisms like natural and acquired resistance. Genetic mechanisms involve inherent and acquired resistance in bacteria, impacting antibiotic effectiveness. Biological resistance mechanisms include enzymatic inhibition, reduced penetration, enhanced extrusion, and target changes. Strategies against antimicrobial agents involve restricting drug entry, modifying targets, rendering drugs inactive, and actively removing drugs from cells. Gram-negative and gram-positive bacteria exhibit variations in resistance mechanisms due to structural differences.

Conclusion

The development of antibiotic resistance in bacteria is a multifaceted issue, involving both inherent and acquired mechanisms. Inherent resistance stems from genetic mutations that occur spontaneously within bacterial populations. On the other hand, acquired resistance can occur through the transfer of genetic material between bacteria, enabling the spread of resistance traits. It is imperative to grasp these genetic, biological, and strategic mechanisms to effectively tackle the escalating challenge of antibiotic resistance and devise successful strategies to mitigate its impact.

Keywords: Microbe, Antimicrobial Resistance, Resistant Mechanisms, Human and Health

Introduction

Antibiotics have played a crucial role in modern medicine, transforming the treatment of infectious diseases and facilitating successful invasive procedures. Their availability has significantly decreased mortality rates and enhanced life expectancy, particularly in children. However, the rise of antibiotic resistance poses a grave threat to global health [1-3]. Humans produce antibiotics for the treatment of infectious diseases. Also, many bacterial species have developed the capability to tolerate

these drugs [4,5].

Sir Alexander Fleming, the discoverer of penicillin, cautioned against the dangers of excessive and inappropriate antibiotic use, which can contribute to the development of resistance [6,7]. More than 50 years ago, the medical community started to recognize the emerging problem of bacterial resistance to antibiotics. Staphylococcus aureus strain had already acquired resistance to penicillin, which was previously an effective treatment for these infections. Resistant bacteria play a crucial role in the occurrence of infections that present significant obstacles in treatment [8]. The issue of drug resistance is exacerbated by the extensive utilization of antibiotics, not only in medical and veterinary practices but also to promote livestock growth [9].

Unfortunately, the prevalence of multidrug-resistant (MDR) bacteria is rising, and the limited supply of new antimicrobial drugs exacerbates the problem. Antibiotic-resistant bacteria have become a significant challenge in healthcare, leading to treatment failures [10]. In response to this urgent issue, governments, along with international organizations such as the World Health Organization (WHO) and the United Nations (UN), have collaborated to combat the development of resistance [11].

However, despite these efforts, the incidence of infections and the spread of MDR bacteria continue to increase. Additionally, the increased utilization of implanted medical devices has resulted in a higher occurrence of infections associated with biofilms, contributing to antibiotic tolerance [12, 13].

The excessive utilization of antibiotics undeniably contributes to the development of resistance [14]. Overuse of antibiotics creates an environment where antibiotics eliminate susceptible bacteria, creating an environment where resistant bacteria can thrive and multiply through the process of natural selection. The epidemiological studies have provided evidence of a direct correlation between antibiotic consumption and the emergence and spread of resistant bacterial strains to these medications. Despite the warnings regarding the excessive utilization of antibiotics, there is still a prevalent tendency to prescribe these medications excessively on a global level [15]. In numerous countries, antibiotics are readily accessible without a prescription, leading to unregulated and widespread usage. The ease of availability and affordability of antibiotics, including online purchasing options, further exacerbate their overuse [15, 16]. The increased utilization of implanted medical devices has resulted in a higher occurrence of infections associated with biofilms, contributing to antibiotic tolerance [12, 13].

In addition, other factors play a significant role in the increasing prevalence of antimicrobial resistance. Antimicrobial drugs are released into the environment through various pathways, including the metabolic processes of hosts and direct application in aquaculture and agriculture [17]. Despite their relatively short lifespan, the continuous and incorrect usage of antimicrobials has resulted in their presence in wastewater, groundwater, and surface water, along with the formation of products during degradation [18,19]. Residues of antimicrobials have been detected in food products such as milk, eggs, and vegetables, leading to prolonged exposure to these compounds [20]. Moreover, scientific studies have highlighted the harmful effects of antimicrobial residues on living organisms [21-23]. Antimicrobials are recognized as a significant contributing factor to the rise and spread of antimicrobial-resistant bacteria (ARB) and antimicrobial-resistance genes (ARGs) [24, 25].

Antibiotic tolerance enables bacteria to survive exposure to antibiotics, even when they are susceptible. Recent studies have revealed that tolerance can precede resistance, and mutations associated with tolerance can lead to the rapid evolution of antibiotic resistance. Therefore, it is imperative to comprehend both antibiotic tolerance and resistance to effectively address the issue of antimicrobial resistance [26-28].

This review aims to summarize how commonly used antimicrobials works and resist. It also presents an analysis of the current status of antimicrobial resistance (AMR) in the most critical bacteria strains, as identified by the World Health Organization's global priority pathogens list.

Material and Methods

The method used in this present article is a literature review with a narrative procedure. This paper includes screening novel studies on the spread of bacterial toxins through food. The international databases PubMed, ScienceDirect, ProQuest, Research Gate, and Google Scholar were utilized for studies as secondary data. Inclusion criteria were available in full text issued in 1929-2021.

Discussion

Antimicrobial resistance (AMR) occurs when microorganisms resist antibiotics, hence its name. This leads to progressing infections becoming severe or palliative, increasing the risk of spreading serious infectious diseases and resulting in potential fatalities. While the overuse of antibiotics is often attributed to the spread of AMR, it is important to note that AMR occurs naturally over time through distinct mechanisms.

Resistance types

Natural resistance

Natural resistance refers to bacteria which are resistant to certain antibiotics, regardless of previous antibiotic exposure. This includes examples such as vancomycin resistance in *Escherichia coli* and cephalosporin resistance in *Pseudomonas aeruginosa*. Natural resistance can also happen due to the bacteria's adapting ability from exposure to medicinal amount of antibiotics.

Acquired resistance

Acquired resistance surfaces from two ways: Mutation and DNA transfer. Mutations can occur in the DNA of bacterial cells during replication and can be passed down to progeny through vertical transmission. Acquired resistance can also happen through horizontal gene transfer, which involves transformation, transposition, and conjugation. In transformation, recipient bacteria take up extracellular donor DNA. Transduction involves a bacteriophage containing donor DNA infects a recipient bacteria. During conjugation or bacterial mating, a donor bacterium transfers its DNA to a recipient. Through these processes, antibiotic-resistant genetic material can be transferred from resistant bacteria to non-resistant bacteria, leading to the development of antibiotic resistance.

Genetic mechanism of antimicrobial resistant

Understanding the mechanisms of AMR is crucial for developing strategies to combat the spread of antibiotic resistance and improve the efficacy of antimicrobial therapies. It is important to address the overuse and misuse of antibiotics in both human and animal settings to slow down the acceleration of this natural process and preserve the effectiveness of antibiotics for future generations.

Inherent resistance

Inherent resistance, which is a natural form of resistance, can be described as a trait that is universally shared within a bacterial species. This resistance arises from spontaneous gene mutations and is not influenced by prior exposure to antibiotics [29, 30]. For example, bacteria like Mycoplasma and related species, which lack a cell wall, are inherently resistant to drugs that target the cell wall, such as β-lactams and glycopeptides [31].

Additionally, certain antibiotics are unable to penetrate the outer membrane of Gram-negative bacteria, leading to intrinsic resistance through this pathway. An example of this is vancomycin, which targets D-alanine-D-alanine peptides in Gram-positive bacteria. However, it cannot penetrate the outer membrane of Gram-negative bacteria, hindering its access to the cell wall [32]. It is important to note that intrinsic resistance is not considered a clinical problem as antibiotics are typically designed to kill vulnerable bacteria [9].

Acquired resistance

Acquired resistance in bacteria involves the development of mechanisms that require either mutating existing genetic materials or the acquiring new genetic materials from external sources [9, 33]. The estimated frequency of spontaneous mutations leading to antibiotic resistance is approximately 108-109, meaning in 108-109 bacteria, one will acquire resistance through mutation [9]. These mutations arise from neglected faulty DNA replication which occur arbitrarily in the genome, often influenced by mutagenic agents. These errors usually dissipates at the cellular or population levels unless they confer a radical benefit to the cell and are transmitted vertically [34]. While mutation is an infrequent occurrence, resistance can emerge relatively quickly in a bacterial population due to the rapid growth rate of bacteria and their replication [35].

Azithromycin, tetracycline, and fluoroquinolones are some of the antibiotics which are ineffective due to spontaneous mutations in *Chlamydia trachomatis*, a major cause of bacterial sexually transmitted infections globally regardless of the country's development status [36].

Biological mechanisms of antimicrobial resistance

Regardless of how a gene undergoes spontaneous mutation or is transferred between bacteria, when the bacteria gene is able to express itself and create an advantageous effect, antibiotic resistance is not impossible. There are four frequently observed mechanisms exhibiting high prevalence in clinical isolates. These mechanisms include:(a) enzymatic inhibition of antibiotic molecules, (b) reduced antibiotic penetration, (c) enhanced extrusion of antibiotics through efflux pumps, and (d) changes in the antibiotic target. This section provides a detailed description of all four mechanisms, the first mechanism being the focus of this paper due to its high frequency and prevalence in clinical isolates [33, 34, 37-42].

Mechanisms of resistance strategies

Resistance mechanisms against antimicrobial agents can be classified into four primary categories: (a) restricting the entry of the drug, (b) modifying the drug's target, (c) rendering the drug inactive, and (d) actively removing the drug from the cell. Intrinsic resistance can utilize strategies such as limiting drug uptake, drug inactivation, and active drug efflux. On the other hand, acquired resistance mechanisms may involve modifying the drug's target, inactivating the drug, or employing drug efflux mechanisms. It is important to note that gram-negative bacteria are different from gram-positive bacteria in their resistance mechanisms due to structural differences. Gram-negative bacteria employ all four main mechanisms, while gram-positive bacteria may less commonly rely on limiting drug uptake (due to the lack of protection from an LPS outer membrane) and may be unable to perform some kind of drug efflux mechanisms [43, 44].

Conclusion

In conclusion, antibiotic resistance in bacteria can be attributed to both inherent and acquired mechanisms. Inherent resistance arises from spontaneous gene mutations, while acquired resistance can result from the transfer of genetic material. Understanding these genetic biological and strategic mechanisms is crucial for addressing the growing problem of antibiotic resistance and developing effective strategies to combat it.

Conflict of Interest

The author declares no conflict of interest.

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