



ANTIBIOTIC MISUSE AND ANTIMICROBIAL RESISTANCE: CURRENT CHALLENGES AND PREVENTION STRATEGIES

Pharmaceutical Science

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ABSTRACT

The reasons for AMR among developing nations are complicated. The reasons may lie within the methods used by the health care professionals, as well as how patients behave in relation to the consumption of antimicrobials, as well as within the chain of antimicrobial supplies. However, the contemporary problems associated with antibiotic resistance are distinct from the past ones, for there have been emerging bacteria that are causing the problem and keep evolving. The emergence of strains that are resistant to several types of antibiotics has not kept pace with the development of new antibiotics. The consequences of antibiotic resistance are grave, with mortality and morbidity continually on the rise. Antimicrobial resistance (AMR) poses a major threat to human health around the world. Some of the contributing factors could be improper drug prescribing, insufficient patient education, inadequate diagnostics, illegal selling of antimicrobials, absence of proper regulation of drugs, and improper use of antimicrobials in animals. In the following paragraphs, we shall explain these health-seeking activities, which result in the emergence of AMR and also look at the healthcare practices that cause AMR in developing countries. Alternative methods of prevention of diseases and other treatment practices should be considered as well.

KEYWORDS

Antibiotic Misuse, Antimicrobial Resistance, Antibiotic Stewardship, Irrational Antibiotic Use, Developing Countries, Public Health.

1. INTRODUCTION

Resistance development in bacteria is happening quickly around the globe and threatens the effectiveness of antibiotics, one of the great inventions of modern medicine that has saved many lives. Many years after the first use of antibiotics for treatment purposes, bacteria once again became a threat. It has been reported that antibiotic resistance has been caused by overutilization of antibiotics, along with the non-development of new drugs by pharmaceutical companies because of economic reasons, as well as complex regulations.[1].

Antimicrobial resistance happens when microorganisms, like bacteria, viruses, fungi, and parasites, gain the ability to survive exposure to antimicrobial agents that used to work against them.[2]. Antibiotic resistance refers to the ability of bacteria to withstand antibiotics. Resistant microorganisms cause treatment failures, longer hospital stays, higher healthcare costs, and increased death rates.[3].

According to the World Health Organisation (WHO), AMR is one of the top ten global public health threats facing humanity [4]. According to recent estimates, antimicrobial resistance was directly responsible for approximately 1.27 million deaths globally in 2019 and contributed to nearly 5 million deaths worldwide [5].

Misuse of antibiotics is among the top causes of AMR. Examples of misuse include self-medication, unneeded prescriptions, wrong dosage, insufficient dosage duration, and use of antibiotics to treat viral infections like the flu and the common cold.[6]. In developing countries, OTC drugs and antibiotics, and poor public awareness further worsen the problem [7].

The role of healthcare professionals, patients, government, and the pharmaceutical industry is critical in tackling the issue of antimicrobial resistance. Strategies that can help curb the abuse of antibiotics include antimicrobial stewardship programs, infection prevention, public health education, and government regulation.[8].

This review aims to discuss antibiotic misuse, the emergence of antimicrobial resistance, current challenges, and evidence-based prevention strategies to combat this growing global health crisis.

2. Antibiotic Misuse

Antibiotic abuse as defined as antibiotic misuse, which leads to antibiotic resistance [9]. Antibiotics may be misused in outside the hospital like by pharmacy store or inside the hospital.

2.1 Self-Medication

Self-medication is defined as a self-practicing drug or over the counter drugs where not involve RMP. Which is leads to antibiotic resistance. [10]

Consequences of Self-Medication

Incorrect diagnosis, Inappropriate drug selection, Drug interactions, ADR, increased antibiotic resistance.

2.2 Inappropriate Prescribing

Doctors often make mistakes with the unnecessary and irrational prescription of antibiotics. The following cases are some common examples:

- Prescribing antibiotics for viral infections
- Using broad-spectrum antibiotics when narrow-spectrum agents are sufficient
- Incorrect dosing and duration
- Polypharmacy [11].

2.3 Incomplete Course of Antibiotics

An incomplete course of antibiotics may lead to antibiotic resistance.[12].

3. Antibiotic-resistant Bacterial Infections

Resistance against antibiotics can be observed all around the world, including the U.S.A. According to the results of the national survey carried out in 2011 among infectious disease specialists through the IDSA Emerging Infections Network, more than 60 per cent of respondents reported their recent experience with a pan-resistant, untreatable bacterial infection. Many agencies of public health refer to the development of antibiotic resistance in bacteria as a "crisis" situation that can lead to "catastrophic consequences." It was stated by the CDC in 2013 that humanity now lives in the "post-antibiotic era," and the WHO in 2014 warned that the problem of drug resistance is becoming extremely critical. MDR bacteria were identified as major threats to public health and national security of the country by the IDSA, Institute of Medicine, and the interagency task force for antimicrobial resistance.

3.1 Methicillin-Resistant Staphylococcus Aureus

The emergence of MRSA was documented some fifty years ago. Since then, infections of MRSA have gone global, manifesting a high prevalence rate in many European countries, along with countries from America and the Asia Pacific regions. Infections of MRSA tend to be quite deadly and among the most prevalent antibiotic-resistant threats. MRSA is responsible for causing 11,285 deaths annually in the U.S. [15].

3.2 Extended-Spectrum Beta-Lactamase (ESBL)-Producing Organisms

ESBL-producing Enterobacteriaceae contain an enzyme known as broad-spectrum beta-lactamase, which allows for resistance to multiple types of antibiotics from the penicillins and cephalosporins families. ESBL-producing Enterobacteriaceae lead to 26,000 hospital-

acquired infections annually, with the death toll reaching 1,700. The problem is that certain strains are almost completely resistant to ESBL-producing bacteria such as *Escherichia coli* and *Klebsiella pneumoniae* are resistant to many cephalosporins and penicillins [16].

3.3 Carbapenem-Resistant Enterobacteriaceae (CRE)

The emergence of carbapenem resistance in Enterobacteriaceae strains with resistance against several other classes of antibiotics has led to the creation of a class of pathogens that is almost universally drug-resistant. The infections caused by CRE have already been shown to cause morbidity and mortality, and these pathogens are making an appearance even among the most vulnerable populations, such as children. CRE are resistant to carbapenems, which are considered last-resort antibiotics [17].

3.4 Drug-Resistant Mycobacterium Tuberculosis

Drug-resistant strains of *Mycobacterium tuberculosis* present a significant problem in the United States as well as on a global scale. As reported by WHO, there were over 170,000 deaths from drug-resistant forms of TB during 2012 alone. Transmission of *M. tuberculosis* typically occurs through airborne routes. TB caused by this bacterium may affect any part of the body, but is mostly found to be localised in the lungs. In 2011, out of 10,528 cases of TB in the US, 1,042 cases had developed drug resistance, which accounted for 9.9% of the total. [18].

4. Current Challenges of Antimicrobial Resistance

Infections caused by antibiotic-resistant pathogenic microbes usually take place in the hospital because there is a congregation of vulnerable individuals and there is extensive use of antibiotics and invasive procedures in hospitals. Evidence shows that up to 50,000 people have died from two types of infections caused by antibiotic-resistant pathogenic bacteria in the year 2006 in America alone: sepsis and pneumonia. These infections have cost the US government about \$8 billion. A trend of indulging in self-medication has also been noticed among the educated population of some developing countries, such as India. As part of research to investigate this phenomenon, it was found that a startling 73% of people in Punjab, a state in India, adopted self-medication to treat minor to recurrent ailments. These observations indicate that despite the identification of a chronic disease, the patients do not regularly consult with medical professionals and assume that they have enough competence to take care of themselves. Besides the commonly observed consumption of antibiotics by a majority of individuals, many people consume drugs like histamine H2-receptor blockers, topical steroids, anti-fungal agents, and oral contraceptives without consulting medical professionals. This clearly indicates a deficiency of knowledge regarding the use of antibiotics and other medications in order to avoid the hassle of going to see a doctor. According to recent research, the practice of self-medication is very common among the poor populations. The health centres in many underdeveloped countries fall short of required standards and are rather expensive, thus making self-medication easier and often essential. There is another reason why self-medication prevails in underdeveloped nations; it is because prescription medications are easily available as over-the-counter drugs. In addition, there are liberal regulations in medicine, which result in the availability of several counter drugs for treating diseases that are prevalent in the area. The major problem that can be faced by the healthcare industry is educating the general public regarding the dangers associated with the misuse of antibiotics, along with the side effects of using such drugs. This problem arises because of the ignorance regarding the use of self-prescribed medications. It has become a matter of great concern as the development of antibiotic-resistant bacteria can cause further serious complications if not tackled now. The problem associated with antibiotic resistance does not remain restricted within the health care sector; however, it may also pose serious threats to the economy of the nation. The next important issue that pharmaceuticals should tackle is that of developing new medicines for treating bacterial infections. The effectiveness of presently available antibiotics is under serious threat because the problems of antibiotic resistance are increasing, and soon bacterial infections will again become life-threatening. Strict regulations and a lack of financial rewards for researchers are some of the factors responsible for this problem because no new medicine has yet been discovered for treating dangerous bacterial infections. [4,6,17]

5. Prevention Strategies

Resistance gene prevalence, once reduced at a local level and accompanied by strict control over the use of antibiotics, will prevent the global problem associated with antibiotics from escalating further.

Insufficient awareness and misconceptions surrounding the use of antibiotics and the resulting consequences should be emphasised in order to effectively deal with the problem. In this case, health professionals have the ability to make a considerable contribution to prevention since patients are more inclined to trust them when it comes to taking medications because of the expertise that they possess. Once a patient receives a diagnosis indicating that he or she requires the use of antibiotics in the treatment process, the health professionals should give detailed information regarding their use, including dose, frequency of the dose, course of the treatment, and the possible adverse effects of their incorrect usage. The failure to properly adhere to a prescribed course of antibiotic treatment and self-medication serves as the leading cause of increased prevalence of medication-induced diseases and the antibiotic resistance crisis. Moreover, health professionals should raise the psychological issues related to adherence to therapy, which include patient education, increased motivation, setting health goals, and increased social support. [6]

6. The Role of Stakeholders in the Control of Antimicrobial Resistance

The fight against AMR should not solely be left to healthcare professionals and researchers. Further education is important for doctors to understand the need to practice rational prescribing and the significance of evidence-based prescribing. The general population and other stakeholders have a central role to play. Every government in the world must make it a priority to tackle AMR in its country. Measures such as policies and regulations have to be established to ensure the responsible access and usage of antimicrobials. The general public has to be made aware of the consequences of AMR, which means that there must be training for media personnel to relay information about medicine and science in simple language to the public. The success of educational programs for journalists on tackling HIV/AIDS issues has worked well for several developing countries, and a similar initiative for AMR would definitely lead to one more positive outcome. Many efforts have already been undertaken by the regulatory authorities and the governments in the fight against antibiotic resistance; however, most of these measures have been implemented in developed nations only. [7]

7. The Clinical and Economic Burden of Antibiotic Resistance

The impact that antibiotic-resistant infections have on the economy and on people's health in the United States is quite serious. They are usually acquired in a hospital because of the concentration of very vulnerable people, many invasive procedures, and the frequent administration of antibiotics in hospitals. Nearly two million patients get HAIs in a year in the USA, leading to the death of 99,000 people; out of which most deaths are caused by antibiotic-resistant strains. It was estimated in the year 2006 that sepsis and pneumonia caused nearly 50,000 deaths in America and incurred losses worth more than \$8 billion.

The problem of antibiotic resistance creates a significant financial burden on the healthcare sector in terms of expenditures. In cases where there is a restriction on the use of first- and second-line antibiotics, healthcare specialists may have to resort to more toxic, often more expensive, medicines. In addition, even if there are effective remedies that can help cope with the infection, statistics indicate that, in general, the number of days needed for recovery from the disease increases by almost twice, which leads to increased expenses on visits to medical institutions. According to calculations, the average hospitalisation period for antibiotic-resistant patients increased by 6.4 to 12.7 days, resulting in an additional 8 million days of hospital stay. [1]

8. How to Control or Reduce Antibiotic Resistance Development

In any case, the most serious side effect of the use of antibiotics is the emergence of resistant strains thereof; this necessitated the introduction of permanent attempts to control the use of antibiotics. Erythromycin is one such example. Used as an alternative to penicillin for *S. aureus* therapy at Boston City Hospital since the beginning of the 1950s, it was immediately withdrawn within less than a year after its introduction due to the fact that more than 70% of *S. aureus* strains showed resistance to erythromycin. This phenomenon was noticed during the use of chlortetracycline and chloramphenicol, and later when other antibiotics were used. Clearly, resistance to antibiotics becomes an inevitable problem to avoid in any way. How can one prevent or, at least, delay the process in question? Several approaches were put forward by knowledgeable specialists and major international health institutions such as the WHO and CDC, among

others. Some of the suggested approaches to the problem include strict control over the human consumption of antibiotics, including mandatory prescription (no antibiotics for colds and other viral diseases), no selling of antibiotics without a prescription (antibiotics should not be used without necessity), and limited application of antibiotics in livestock and agriculture. It is interesting to note that Swann Recommendations of 1969 were the first to suggest the prohibition of non-therapeutic use in farm animals and in agriculture, which was a quite reasonable and highly controversial proposal that proved to be impossible to put into practice even in today's world. Deception also played its role here since the majority of antibiotics that are used in humans are prescribed for animals under other names, as is indicated in The Report of the Advisory Committee on Animal Antimicrobial Use Data Collection in the United States of the Alliance for the Prudent Use of Antibiotics. While the Netherlands and Scandinavian countries managed to lower resistance rates considerably, it is obvious that limiting the use of antibiotics on a worldwide level is an unachievable task. The universal acceptance of proposed limitations and restrictions would definitely result in positive outcomes, but would the problem of resistance be solved then? Definitely not. Please see the latest report (one among many), "Antibiotic Resistance: an Ecological Perspective on an Old Problem". However, in case when reasonable limitations and rules are accompanied by structural novelties in antibiotic and semi-synthetic compounds' development, the expected results will be considerable. [14]

9. Future Perspectives

Research papers and popular mass media have continuously warned people regarding the danger of antimicrobial resistance. Scholars have shown anxiety over the increasing trend in the number of people infected with invasive diseases caused by multidrug-resistant bacteria (MDR) and the rise in the mortality rate from these diseases. Hence, it is necessary to stress that there is an urgent need for researchers to develop new antibiotics because there is an increasing trend in the number of pan-drug-resistant bacteria, which is a dangerous situation resulting in millions of deaths around the world. Nevertheless, there is another aspect of this discussion as well, since the level of resistance to certain categories of antibiotics in the MDR phenotype has been quite constant and low, while other alternatives are available to old antibiotics. The number of mortalities related to MDR bacteria is controversial because not all cases are reported, and mortality rates are high even from non-MDR bacteria. According to some scholars, the existing antibiotics will be sufficient to deal with the challenge of emerging bacterial resistance as long as the diseases are controlled on a nonprofit basis internationally.

One Health is an approach that recognises that the health of people is closely connected to the health of animals and our shared environment, addressing AMR.[6]

10. CONCLUSION

The growing issue of antibiotic resistance poses dangers to the impressive health gains that have been made possible through the use of antibiotic medications. While the drug manufacturing firms remain unresponsive to this growing crisis by not inventing any new drugs to fight against microbial infection, the antibiotics are still being overprescribed around the globe, thereby resulting in the antibiotic resistance phenomenon becoming a major global health problem. Not only does this crisis constitute a major health hazard for the drug industry and healthcare industries, but it also constitutes a significant economic problem for the world.[7]

The quick emergence of these antibiotic-resistant pathogens poses a threat to all the remarkable achievements made possible by using antibiotics. This is a situation that affects the whole world because of the excess use of antibiotics and insufficient creation of new ones to counteract the problem. These infections cause high costs for the American healthcare system and its people.[6]

The lack of antimicrobials will have dire consequences on the efficiency of various medical procedures, such as surgical interventions, the management of preterm infants, cancer treatments through chemotherapy, critical care medicine, procedures of diagnosis and treatment, and transplantation medicine, because there will be increased mortality rates due to secondary infections. Global resistance to antimicrobials is similar to that of global warming or climate change. Thus, while working to ensure that the climate does not become hazardous to the next generation, it is our moral obligation

not to allow the next generation an environment that has microorganisms resistant to their treatments because the effects could be extremely catastrophic.[1]

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