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Review Article

Development of Antibiotic Resistant Strains in Bacteria

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Abstract

It is been seen that most of the common bacteria are getting resistance to antibiotics. This review article is based on the development of this resistance in the respective organisms. Most commonly known bacteria like *Mycobacterium tuberculosis, Staphylococcus aureus, Escherichia coli, Clostridium perfringens, Campylobacter* sp., *Klebsiella pneumoniae, Burkholderia cenocepacia* etc. are some of the species included in the list of developing the resistance and thus causing some threatening diseases. So there is an urgent need of some new set of antibiotics which can kill these resistant strains of bacteria. World Health Organization (WHO) has began to design new projects on discovery of drugs or alternative therapies against these resistant strains of bacteria. This includes various approaches of treatment including immunotherapy and nanoparticles.

Keywords: *Antibiotic; Resistant Strains; Bacteria*

Introduction

The discovery of penicillin by Sir Alexander Fleming in 1928 led to the modern era of antibiotics [1]. After this discovery, antibiotics have transformed modern medicine and millions of lives were saved [2]. Bacterial infections have again become a threat after so many years since the first patients had been treated with antibiotics [3]. There can be many ways by which resistances are developed in bacteria. The overuse scince antibiotics actually drives the evolution of resistance [4]. Antibiotic-resistant infections are increasing in children nationally and globally. This is primarily due to the selective pressure created by the broad use of antibiotics [5]. The horizontal gene transfer (HGT) also allow antibiotic resistance to be transferred among different species of bacteria [4]. Sometimes incorrectly prescribed antibiotics expose patients to potential complications of antibiotic therapy, which can also led to antibiotic resistance [6]. Sub inhibitory and sub therapeutic antibiotic concentrations also promote the evolution of antibiotic resistance as they support genetic alterations, such as changes in gene expression, HGT, and mutagenesis [7]. It has been seen that the antibiotics used in livestock are transferred to humans when they consume food. This transfer of resistant bacteria to humans by farm animals was first seen 35 years ago, when high rates of antibiotic resistance were found in the intestine of both farm animals and farmers [8]. Bacteria also produce enzymes that inactivate the drug by adding specific chemical moieties to the compound or that destroy the molecule itself, in the presence of antibiotics. Thus rendering the antibiotic incapable of interacting with its target. An example of enzymatic alteration of an antibiotic is the modification of chloramphenicol. Bacterial plasmids have also served as scaffolds on which an exchange of multiple antibiotic resistant genes occurs [9].

Results

Because of the high resistance level of *Mycobacterium tuberculosis* to antibiotics and the newly acquired mutations which confer further resistance, the treatment of tuberculosis (TB) has been a therapeutic challenge [10]. The resistance shown by *M. tuberculosis* is due to spontaneous chromosomal mutations. It has been seen that well-designed combination of drugs under supervised therapy can prevent the emergence of drug-resistant strains [11]. The therapeutic agents actually disrupt the DNA replication cycle of *M. tuberculosis*. Replication involves two steps, i.e. breakage and reunion of DNA at gyrase A (GyrA) domain and ATP hydrolysis at gyrase B (GyrB) domain. Current therapy for multi-drug resistant TB (MDR-TB) involves, fluoroquinolone-based antibiotics, which targets replication process at GyrA domain. Due to the mutation in the GyrA domain we have shifted the focus on GyrB domain. Now using in silico techniques novel chemotherapeutic agents for resistant TB are designed [12].

Staphylococcus aureus is a gram-positive, sphere-shaped (coccal) bacteria which cause skin infections but can also cause pneumonia, heart valve infections and bone infections. *Staphylococcus aureus* (*S. aureus*) is a major cause of infection in hospitals and within communities across the world. It is seen that it has developed resistance to commonly prescribed antimicrobial agents [13]. Out of 1789 S. aureus isolates analysed, four isolates were found resistant to vancomycin and were confirmed as VRSA (vancomycin-resistant *Staphylococcus aureus*) based on MIC results and *vanA* gene detection. Nearly six strains were found to be methicillin-resistant [14].

E. coli mostly causes urinary tract infections [15]. When the *E. coli* antimicrobial resistance in 556 first urine samples of the day from outpatient population of Hrasno community in Sarajevo, Bosnia and Herzegovina was taken, it was observed the antimicrobial resistance of *E. coli* for ampicillin was (82.79%), followed by trimethoprim-sulfamethoxazole (40.86%), nalidixic acid (19.35%), cephazolin (7.52%), nitrofurantoin (5.37%), gentamicin (2.15%) and ciprofloxacin (4.30%). This results showed that *E. coli* has the highest resistance to ampicillin and trimethoprim-sulfamethoxazole in outpatient population of Hrasno community [15]. The resistant strains of *E. coli* was found to be higher in frequency among female outpatients of Hrasno community [16].

Clostridium perfringens, a Gram-positive bacteria creates variable pathogenic condition, ranging from a food poisoning to life-threatening myonecrosis. From 136 stool samples including diarrhea (48) and non-diarrhea (88) patients, *C. perfringens* were cultured. In 79 isolates of *C. perfringens*, 34 cases showed no resistance, 18 had one resistance and 27 isolates had multiple resistance to imipenem, metronidazole, ceftriaxone, clindamycin, chloramphenicol, and penicillin [17].

Campylobacteria sp. is still an important cause of diarrheal disease all over the world. It is also showing resistance towards antibiotics [18]. In *Campylobacter*, a resistance-enhancing variant (named RE-CmeABC) of the predominant efflux pump CmeABC has led to the development of antibiotic resistance characterized by increased MICs and decreased levels of accumulated intracellular antibiotics [19].

Klebsiella pneumoniae is a multidrug resistant (MDR) organism. It is considered as urgent threat to human health by the World Health Organization, the US Centers for Disease Control and Prevention and the UK Department of Health. The resistance to colistin and polymyxin B is developed due to the deletion of the *mgrB* gene [20].

In species like *Burkholderia cenocepacia*, a specific lipocalin is produced which helps the organism to survive against the antibiotics. It was seen that on exposure to sublethal concentrations of the drug, lipocalin increased the resistance of the organisms [21].

Several cases of antibiotics abuse have also been reported. Use of tumor necrosis factor inhibitor in certain cases has led to the development of increased infection in some auto immune patients. Multidrug-resistant *Acinetobacter baumannii* (MDRAB) pneumonia is one of them. TNFI affects the mucosal immunity and thus contributes to *A. baumannii* colonization and further development of MDRAB in frequently hospitalized patients [22].

Conclusion

Through various experimental operations, it has been seen that there is a constant need for new drugs as majority of the microbial population has started developing resistance. As discussed before, these developments can come from the plasmid via conjugation as it serves as a gene pool for antibiotic resistance genes or may develop due to constant antibiotic abuse. It has been seen in various studies that presence of certain elements helps the antibiotics to work better. For example, ZnO nanofluids improves the *in vivo* antibacterial activity of ceftazidime whereas keeps the activity of ciprofloxacin unaltered at similar conditions [23]. *Mycobacterium tuberculosis* (Mtb) strains have also been known to develop antibiotic resistances. Recent approaches include designing of a multi-antigenic and multiphasic vaccine, based on the Modified Vaccine Ankara (MVA) virus, denoted by MVATG18598. The immune therapy involving it basically comprises of the release of ten antigens which each corresponds to the different phases of the Mtb infections, thus preparing the body against the respective antigens [24]. Since the development of antibiotic resistance in bacteria is becoming a very serious problem. A cell of World Health organisation is trying to organise new projects for the discovery of new drugs to curb this growth.

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