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Delving Into Antibiotic Resistance: The Why, How, And When

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INTRODUCTION

In recent times, antibiotic resistance of pathogens to drugs (antibiotics) directed towards the degrading properties of microbes in vivo has been on the increase both in the community and in the hospital. Antibiotics are exceptionally vital in clinical medicine for the treatment of bacterial related infections, but unfortunately bacteria are capable of developing resistance to them. Antibiotic resistance is a global health problem that has bedeviled our health sector worldwide, affecting both the developed and developing countries of the world. They make infectious diseases very difficult to treat. The emergence of antibiotic resistance is a complex problem that is driven by many interconnected factors, of which the use and misuse of antimicrobial agents (antibiotics, antiseptics, disinfectants, and preservatives) amongst other factors, is the main driving force for the development of resistance. There is therefore a need to step up the process of discovering and developing novel antibiotics that will be stable to the evolving resistance nature of microbes (1).

WHAT ARE ANTIBIOTICS?

There is no consensus to the definition of antibiotics. But it is very important that we do not displace the key points (“Killing and Inhibition”) that must be contained in any definition of an antibiotic. Abinitio, an antibiotic was originally defined as a substance produced by one microorganism, which inhibits the growth of other microorganisms. But due to the development of other synthetic or chemical methods by which drugs can be produced, there has been a modification to this definition (2). Today, an “antibiotic” can be defined as a substance produced by a microorganism (wholly or partly by chemical synthesis), which in low concentrations kill or inhibit the growth of other microorganisms in vivo or in vitro. The discovery of antibiotics and their subsequent application to clinical medicine is one of the outstanding scientific achievements of the twentieth century. Antibiotics have been used for about six decades now to treat and cure variable series of diseases including tuberculosis, pneumonia, gonorrhea, urinary tract infections (UTI’s), respiratory infections, syphilis, and other microbial related diseases, and they have been found to be very efficacious in this aspect.

There are several classification/types of antibiotics today, which is based on bacterial spectrum of activity (whether broad or narrow) or type of activity exhibited by the agent (whether bactericidal or bacteriostatic). Some antibiotics are also classified based on their chemical structure. And this leaves antibiotics within a particular structural class to have similar patterns of effectiveness, toxicity, and allergic potential.

HOW ANTIBIOTICS WORK

The majority of antibiotics exert a highly selective toxic action upon their target microbial cells but have little or no toxicity towards mammalian cells. These antibiotics can therefore be administered at concentrations sufficient enough to kill or inhibit the growth of infecting organisms without damaging mammalian cells. The ways by which these antibiotics exert their antibacterial activities on their target microbes in vivo without necessarily harming the host (patient) taking the drug is called the “Mechanism of Action of Antibiotics”. It reveals and explains the rationale behind the selective toxicity of antibiotics and how they stop the venomous effects of bacteria. Selective toxicity is the ability of antibiotics (antimicrobial agents) to kill or inhibit the growth of microorganisms (*in vivo*) without causing any untoward effect to the host taking the agent (drug). It is the ability of an antimicrobial agent

to kill or inhibit a microbial pathogen while damaging the host as little as possible. For antibiotics to be therapeutically relevant for use against a particular pathogen in vivo, it must be selectively toxic in nature. Antimicrobial agents (in particular antibiotics) show a wide variety of mechanisms of action against pathogenic microorganisms either in vivo or in vitro; and these shall be discussed in this section.

IDEAL PROPERTIES OF ANTIBIOTICS

There are three essential characteristics of antibiotics, these are: *in vivo* as well as*in vitro* effectiveness, lack of toxicity, and reasonable cost to the healthcare system.*In vitro* activity is dependent upon the ability of the antimicrobial agent to reach its microbial target site and to overcome various mechanisms of resistance in the infecting organism. In addition to possessing*in vitro* activity against the infecting organism, effective drugs must penetrate to the site of infection and must retain significant activity at that location.

HOW DOES ANTIBIOTIC RESISTANCE OCCUR?

Antibiotic resistance occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals or agents designed to cure or prevent the infection. Thus, the bacteria survive and continue to multiply causing harm and havoc in the patient (host) taking the drug. There has been a very great concern that the “antibiotic era” might be coming to an end – firstly, because the rate of production of new drugs has diminished greatly and, secondly, because microbes (viruses, bacteria, fungi, protozoa) are showing great inventiveness in devising mechanisms for circumventing the inhibiting and killing properties of drugs (antibiotics) directed towards them. Deaths from acute respiratory infections, diarrheal diseases, measles, malaria and tuberculosis account for more than 85% of the mortality from infection worldwide (3).

Antimicrobial resistance often occurs due to gene transfer, meaning that some organisms of a population are resistant to a certain antimicrobial, whereas others are not (4). This can be a spontaneous or induced mutation. Many antibiotic resistance genes reside on transmissible plasmids (a small DNA molecule that is able to replicate independently of the chromosomal DNA contained within a cell), facilitating their transfer (5). Exposure to an antibiotic naturally selects for the survival of the microorganisms that possess the genes for resistance. Based on this, a gene for antibiotic resistance can potentially spread through a bacterial ecosystem. The phenomenon of antimicrobial resistance has been accelerating over the past three decades. The causes of antimicrobial resistance include the over-prescribing by doctors, indiscriminate use on farm animals, and public misuse, such as sharing antimicrobials.

Irrespective of the fact that pathogenic microorganisms have developed resistance genes or traits that allow them to dodge the antimicrobial onslaught of these agents or drugs, antimicrobial agents (inclusive of antibiotics) with their therapeutic prowess are still invaluable for the management and treatment of diseases caused by pathogenic organisms. However, antibiotic resistance is a growing threat and the need to find new and novel compounds is pressing (6).

HOW EXTENSIVE IS ANTIBIOTIC RESISTANCE?

Resistance of microbes to first-line drugs causing these diseases according to the WHO ranges from zero to almost 100% and in some cases, resistance to both second – and third – line drugs is seriously compromising treatment outcome. A major example is extended spectrum ? – lactamase (ESBL) – producing bacteria which is resistant to virtually all beta – lactam drugs and some non – beta lactam drugs. Antibiotic resistance though a natural biological phenomenon, has in no doubt lead to the loss in the efficacy of some important drugs (especially the beta-lactams) from our therapeutic armamentarium. Nobody is to be blamed for this plethora of menace that is gradually eroding the efficacy of our drugs, since the introduction of every antimicrobial agent into clinical practice at one time or the other has been followed by the detection in the laboratory of strains of microorganisms that are resistant to these antimicrobial agents.

TACKLING THE RESISTANCE

Finding new medicines to kill pathogenic bacteria is becoming more difficult. Some scientists are trying to adapt tried-and-true antibiotics to discover other usable treatments out of them. Other researchers are looking for new compounds that can be used as templates to develop medicines. Whereas other research centers are plumbing the unexplored crevices of bacterial physiology, hoping to unearth targets that could lead to whole new classes of antibiotics. A parallel areas is with minimizing use and over-use of current antibiotics through community controls (7).

In containing antibiotic resistance in both the community and the hospital, a good and adequate routine diagnostic antimicrobial susceptibility testing in the microbiology laboratory is paramount. Clinical microbiologists should be charged with the responsibility of detecting antibiotic resistant strains of microbes in the hospitals and in the community using internationally recognized protocol as outlined by the Clinical and Laboratory Standard Institute, CLSI (formerly, National Committee for Clinical Laboratory Standards) guideline. Data emanating from such studies should be made available and harnessed properly by all stakeholders in order to develop a road map for the proper control and eradication of antibiotic resistance from our world. Therefore, it is important for us to close the door on antibiotic resistant strains of bacteria before we wake up someday and find out that the only weapon (antibiotics) we have against bacterial related diseases have left us.

Due to the rise in the increase in treatment-resistant bacterial pathogens in both inpatient and outside of the healthcare setting, and given the problems with finding alternative antibiotics, most clinicians are advised to evaluate if an antibiotic is needed and how it should best be utilized to achieve treatment success while also minimizing unnecessary exposure and creating so-termed “collateral damage” to the microbiome.

CONCLUSION

Antibiotics and antimicrobials have served humanity well across six decades. However, the rise of antimicrobial resistance has created the pressing need for a global strategy. This will involve humanity conserving the antibiotics left by using them optimally (this is sometimes referred to as ‘antimicrobial stewardship’). Secondly, the process of developing new antimicrobials and new technologies to allow quicker diagnosis and facilitate targeted treatment must be accelerated, and this requires governmental support

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