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Review Article

Antibiotic Resistance –An Overview

Reeja Pappachan*, K. Krishnakumar, L. Panayappan, Rosmin Jacob*
Department of Pharmacy Practice, St James College of Pharmaceutical Sciences, Chalakudy, Kerala
St James Hospital Trust Pharmaceutical Research Centre (DSIR Recognized), Chalakudy, Kerala

***Corresponding author**
Reeja Pappachan
Email: stjamespharmacyproject@gmail.com

Abstract: Antibiotic resistance is one of most serious health problem. Infections from resistant bacteria are now common. Some pathogens are even become resistant to multiple types of antibiotics. The extraordinary genetic capacities of microbes have benefitted from man's overuse of antibiotics to exploit every source of resistance genes and all means of horizontal gene transmission to develop multiple mechanisms of resistance for each and every antibiotic introduced into practice clinically. The shortage of effective antibiotics will lower the capability to fight infectious diseases. This mainly affect the management of infectious complications in high risk patients undergoing surgery, especially organ transplantation. To prevent the antibiotic resistance by the strict controls on antibiotic use by humans.
Keywords: Antibiotic resistance, Infections, Mutation.

INTRODUCTION

The ability of the bacteria and other micro-organisms to resist the effect of antibiotic to which they were once sensitive and continue to multiply in the presence of therapeutic levels of an antibiotic is called Antibiotic Resistance. Antibiotic resistance is a major health problem. This condition makes it harder to eliminate infection from the body as a result of a bacteria's ability to survive in the presence of antibiotics, some infectious diseases are now more difficult to treat and leads to treatment complications and increased healthcare costs. The misuse of antibiotics is the single most important factor that leads to antibiotic resistance around the world. The use of antibiotics without infections creates resistance. These drugs should only be used to manage infections. When the first and second-line antibiotic treatment options become restricted due to resistance or unavailability, healthcare providers are forced to use antibiotics that may be more toxic to the patient. These antibiotics tend to be more expensive and less effective. Even with alternative treatment, patients having resistant infections have either died or have had a significantly longer hospital stay, delayed recuperation, and long-term disability. Drug resistant strains initially appeared in hospitals where most antibiotics were being used; for example Sulfonamide resistant streptococcus pyogenes emerged in 1930s,Penicillin resistant staphylococcus aurous developed soon after the introduction of penicillin similarly mycobacterium tuberculosis came with resistance to streptomycin soon after the usage of antibiotic.

Resistance to multiple drugs was first detected among enteric bacterialike E. coli, Shigella and Salmonella, in the early 1960s. Such resistance among various microbial species to different antimicrobial drugs is a cause of public health threat all over the world at a terrifying rate. The emergence of MultiDrug Resistance (MDR) is clearly related to the mismanagement of antibiotics. It also reflects attainment of different resistance determinants on the same DNA molecule, or single determinants, such as multidrug pumps, that specify efflux activity against different antibacterial [1].

Problems of resistance

Antibiotic resistance infections double the duration of hospital stay, double mortality and probably double morbidity when compared to drug susceptible infections. A cost comparison of treating Methicillin resistant (MRSA) vs. Methicillin susceptible (MSSA) S. aureus found almost a threefold increase in mortality (21% to 8%) and an economic cost increase of 22% associated with MRSA. In United States and United Kingdom, 40-60% of nosocomial S. aureus strains are Methicillin resistant and usually MDR. More deaths are associated with MRSA than with MSSA strains. Small proportions of MRSA show a steady increase in low level resistance towards Vancomycin, leading to failure in treatment. Among the gram-negative bacteria,

hospital infection caused by P. aeruginosa and A. baumanii are sometimes resistant to all, or all but one antibiotics, which seriously challenge the treatment of immunocompromised individuals and can result in death. The extended spectrum beta Lactamases, carried among Enterobacteriaceae such as Enterobacter and Klebsiella, destroy even the latest generations of Penicillin and Cephalosporin. Today, MRSA strains that differ from the hospitals strains and possessing new virulence toxins (Panton-Valentine Leukocidin) have emerged in communities of industrialized countries. The so called community acquired MRSA is resistant to β-lactam antibiotics, requiring physicians to prescribe alternative therapies where MRSA is suspected. Children were found to be more community acquired MRSA infection because the disease had advanced by time that another effective therapy was initiated [2].

Causes of antibiotic resistance

There are two main mechanism involved in the development of antibiotic resistance namely mutation and acquisition of resistance genes by horizontal gene transfer (HGT). The genes for resistance properties can get transferred between bacteria of different taxonomic and ecological groups by means of mobile genetic elements such as Bacteriophages, Plasmids and Transposons. These genes are generally directed against a single type of antibiotic, although multiple genes, each bearing asingle drug resistance trait, can accumulate in the same organism. In the absence of plasmids and transposons, bacteria gain a steady increase in resistance through mutations in chromosomes. This process was primarily responsible for the exposure of penicillin and tetracycline resistance in N. gonorrhoeae. The organism later obtained transposons bearing genes with high level resistance to those drugs. Strains of E.coli and other Enterobacteriaceae have develop increasing resistance to Fluoroquinolones, as the result of mutations in the target enzymes (topoisomerases) and an increase in the bearing of membrane proteins that pump the drugs out of the cell [3].

In antibiotic resistance, Genes will be transferring between bacteria in a parallel manner by conjugation, transduction, or transformation. Thus a gene for antibiotic resistance which had developed by means of natural selection may be shared. Many antibiotic resistance genes occupy on plasmids, ease their transfer. If a bacterium carries several resistance genes it is called multi-resistant or informally a superbug or super bacterium. The extraordinary genetic capabilities of microbes have has evoked resistance genes that helped develop multiple mechanisms of resistance against antibiotics introduced into practice clinically [4].

The long-term use of a single antibiotic (for more than 10 days) will make that bacteria resistant not only to that antibiotic but to many others. This phenomenon was found to occur after the continuous use of tetracycline in the urinary tract infections. Under continued antimicrobial selection, the susceptible intestinal flora may become colonized by organisms that are resistant not only to the absorbed drug, but also the structurally unrelated drugs. In animals MDR appeared after the application of sub-therapeutic (growth promotion) levels of Tetracycline in their feed. Within days, chickens began excreting tetracycline-resistant E. coli; by two weeks, the excreted E. coli was resistant to several antibiotics.

Selection of combinations in antibiotic resistance

The analysis of the structure and functional relationship lead to the development of antibiotic resistance property. For example, the therapeutic action of β-lactams is achieved by binding to PBPs thus demolish the growth and structural integrity of bacterial cell walls. B-lactamases have similar structure to Penicillin Binding Proteins that play an important role in bacterial cell cycle. The transpeptidation reaction conducted by PBPs is used to stabilize the cell wall by cross-linking the glycan strands during peptidoglycan synthesis. The structural modifications during the development of the intermediate antibiotic resistance enzyme were due to the loss of interaction with the peptidoglycan moieties. The wide distribution in the environment and efficient catalytic properties of β-lactamases has probably served as arbitrator in β-lactam cross-talk for a long time.It is not surprising that these genes were quickly picked up from the environmental genetic reservoirs and dispersed into commensal and pathogenic microbiota following the introduction of β-lactam antibiotics into clinical practices [5].

Prediction of antibiotic resistance

Initially, experiments proceeds towards to predict the evolution of antibiotic resistance genes have included in vitro evolution modeling and screening for cryptic antibiotic resistance genes. A broader conceptual framework to predict antibiotic resistance was proposed, that included many variables such as the estimates of potentiality and prospect affecting the actuality, e.g. the real antibiotic resistance in bacterial populations. Genetic mechanisms that may contribute to evolution of antibiotic resistance. There is no official framework for predicting antibiotic resistance, primarily due to the lack of knowledge in several key areas such as the true extent of microbial metabolic diversity that may grant to novel antibiotic resistance, the rates of mutation and horizontal gene transfer (HGT) in a natural ecosystems, and the range of genetic interaction between different ecosystems. The situation of antibiotic resistance development that are based on insufficient knowledge in an attempt to protect the

efficacy of novel antibiotics The first and second generation of Tetracycline (called Glycylcyclines) have gradually lost their efficiency due to the widespread resistance mainly by the ribosomal protection and efflux mechanisms. However the third generation of Tetracycline, Tigecycline (the minocycline derivative 9-Tert-Butyl-Glycylamidominocycline) was approved by the US Food and Drug Administration (FDA). This antibiotic was very effective against the bacterial isolates that contained the two major determinants that are responsible for Tetracycline resistance. Thus it is a valuable therapeutic option when dealing with difficult to treat superbug's infections such as Methicillin-resistant Staphylococcus aureus (MRSA), Vancomycin-resistant Enterococci (VRE), Penicillin resistant Streptococcus pneumoniae and the β-lactamase producing Enterobacteriaceae. We can conclude that the influence of resistance to Tigecyclinein pathogenic microbiota is very low at this time [6].

How to reduce the antibiotic resistance development

The serious outcome of the use of antibiotics is the associated development of resistant strains. A continuous control effortneeds to be exerted over antibiotic usage. Erythromycin was an example; introduced as an alternative to penicillin for the treatment of *S. aureus* in the early 1950s, it was completely withdrawn within few months because 70% of all the *S. aureus* isolates were found to have become erythromycin resistant. The same trend was observed with chlortetracycline and chloramphenicol, also with other antibiotics. It is clear that antibiotic resistance looks unavoidable but steps can be taken to prevent or cause a delay in the resistance by implementing strict controls over the use of antibiotic by humans, dispensing antibiotics with accurate prescriptions (not to use antibiotics to treat colds and other viral infections), don't take antibiotics without a doctor's prescription and a controlled therapeutic use in animal husbandry and agriculture. A related scheme involves treatment with combinations of inhibitory compounds that have different modes of action. This combinatorial approach (a Flouroquinolones plus a macrolide or a β-lactam plus an aminoglycoside or tetracycline) has been used in the past to overcome resistance and has also been used with success in the treatment of diseases such as cancer and HIV infection. The development of conjugated vaccines, such as those based on encapsulated H. influenzae type-b and pneumococcus, can reduce bacterial disease and the resulting need for antibiotics [7].

CONCLUSION

Antibiotic misuse is a global treat because of the spread and development of resistance in most common bacteria to most inexpensive generic antibiotics. Now antibiotic resistance is universally recognized as a public health priority and necessary plan of action to combat resistance should be developed. Better diagnostic tests, encouragement and evaluation of medical and veterinary practice guidelines, restriction of antibiotic use as growth promoters in foods and animals, development of novel antibiotics are some of the steps required [7]. Above all, patients, health providers and health care leaders must make a serious dedication to change the dynamics of outpatient prescribing. If we want to prove the prediction of an impending post-antibiotic era wrong, the time has come to drastically improve our antibiotic prescribing practices and to strengthen research to identify cost-effective strategies for controlling resistance. If this could be achieved, the care of an individual patient at large can be substantially improved.

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