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RESEARCH ARTICLE

An Overview on Antibiotic use and resistance

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ABSTRACT:

Antibiotic resistance is a very important challenge to the Medical Staffs in the treatment of infectious diseases. Over the recent years many papers have been published regarding Antibiotic uses and its resistance. We have referred various articles which have published on the uses of antibiotics, over the counter drug use, multi drug resistance, gene transfer and epidemiological studies and based on that we have prepared a mini summary which has been highlighted particular on the integration of data, uses, causes of resistance and mechanism of action of antibiotics in this article.

KEYWORDS: Resistance, Mechanism of action, Infectious diseases.

INTRODUCTION:

Decades ago, Since the introduction of antibiotics it was considered as “wonder drugs,” primarily because of their life-saving benefits in treating serious wounds, postsurgical infections, pneumonia, meningitis, endocarditis, and sepsis, as well as their dramatic effect on sexually transmitted infections and infections of the urinary tract¹. Medical Experts have taken comfort in the relative safety and exceptional efficacy of these drugs. Antibiotics are available for use in the form of oral as well as parenteral formulations². It has been used enthusiastically by physicians, and patients have benefited in the therapy of several diseases, even those which is not known to be caused by bacteria. It is widely believed that more than half of the population use of antibiotics is for the treatment of respiratory infections in children, well more than half of which are caused by viruses.

The modern era of antibiotics started with the discovery of penicillin by Sir Alexander Fleming in 1928 and saved millions of lives. Penicillin was successful in controlling bacterial infections and penicillin resistance became a clinical problem, by the 1950s. Antibiotics were prescribed to treat serious infections in the 1940s. The therapy of microbial infections in ancient times of other countries is well-documented³.

It has been documented not only against antibiotics of natural and semi-synthetic origin, but also against purely synthetic compounds (such as the fluoroquinolones) or those which do not even enter the cells (such as vancomycin). The wide range of occurrence of antibiotic resistance suggests that, in principle, any organism could develop resistance to any antibiotic. The phenomenon of horizontal gene transfer compounds the problem by facilitating rapid spread of antibiotic resistance. Unfortunately, the discovery and development of newer antibiotics have not kept pace with the emergence of antibiotic resistance⁴. Since then, antibiotics have transformed modern medicine and however, shortly thereafter, many of the advances of the prior decade were threatened. In response, new beta-lactam antibiotics were discovered, developed, and deployed, restoring confidence. However, the first case of methicillin-

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resistant *Staphylococcus aureus* (MRSA) was identified during that same decade⁵, in the United Kingdom in 1962 and in the United States in 1968.

USES OF ANTIBIOTICS:

Antibiotics have successfully prevented or treated infections and not only saved patients lives, They have also played a important role in achieving major advances and developments in Medicine and Surgery⁶. It helped to extend expected life spans by therapeutically changing the outcome of bacterial infections. The average life span of people using antibiotics in life threatening conditions has increased. In few developing countries where sanitation is still poor, morbidity and mortality due to food and poverty related infections, antibiotics are having beneficial uses both therapeutically and also economically. People at risk of bacterial infections. Antibiotics are sometimes given as a precaution to prevent, rather than treat, an infection. This is known as antibiotic prophylaxis. It is normally recommended if you're having surgery on a certain part of the body which carries a high risk of infection or where infection could lead to devastating effects. In case of bites or wounds that has a high chance of becoming infected⁷.

MECHANISM OF ACTION OF ANTIBIOTICS:

The five major mechanism activities of antibiotics are It interferes with Cell wall Synthesis for example Beta-lactam antibiotics like Penicillin and Cephalosporins inhibit the enzymes that are responsible for the formation of peptidoglycan layer. Then, Protein synthesis inhibition for example Oxazolidinones, Tetracyclines interfere with protein synthesis by binding to 30S subunit of ribosome, thereby weakening the ribosome-tRNA interaction. Macrolides, Chloramphenicol bind to the 50S ribosomal subunit, inhibit the elongation of polypeptide chains and also blocking peptidyl transferase reaction. Aminoglycosides inhibit initiation of protein synthesis and bind to the 30S ribosomal subunit⁸.

Interferes with nucleic acid synthesis for example Rifampicin interferes with a DNA-directed RNA polymerase. Quinolones inhibit DNA synthesis with interference of type II topoisomerase, DNA gyrase and type IV topoisomerase during replication cycle causing double strand break. Then, Inhibition of a metabolic pathway for example Sulfamethoxazole and Trimethoprim each block the key steps in the folate synthesis, which is a cofactor in the biosynthesis of nucleotides, the building blocks of DNA and RNA. the primary site of action is the cytoplasmic membrane of Gram-positive bacteria, or the inner membrane of Gram-negative bacteria and also Disorganizing of the cell membrane for example It is said that polymyxins exert their inhibitory effects by increasing bacterial membrane permeability, causing leakage of bacterial content. The

cyclic lipopeptide daptomycin displays rapid bactericidal activity by binding to the cytoplasmic membrane in a calcium-dependent manner and oligomerizing in the membrane, leading to an efflux of potassium from the bacterial cell and cell death⁹.

REASONS FOR ANTIBIOTIC RESISTANCE:

Despite the efforts to improve antibiotics, bacteria continue to evolve in response to the drugs they are exposed to, and in many cases the organisms present in the environmental ready possess resistance to antimicrobials there are still in the approval process by FDA¹⁰. Each time a drug is prescribed to a patient, all bacteria whether is the target of infection or not are reached, causing a survival pressure over these bacteria, leading to the rise of antimicrobial resistance, which is an evolutionary process characterized by the competition between the resistant and sensitive strains. The processes can occur, individually; in patients, asymptomatic populations or in the environment¹¹.

The overuse of antibiotics is clearly the main reason for evolution of resistance. There are many articles which published and we have surveyed few related to Epidemiological studies which have demonstrated a direct relationship between antibiotic consumption and the emergence and dissemination of resistant bacteria strains. In bacteria, genes can be inherited from relatives or can be acquired from nonrelatives on mobile genetic elements such as plasmids. This horizontal gene transfer (HGT) can allow antibiotic resistance to be transferred among different species of bacteria.¹² Resistance can also occur spontaneously through mutation. In many other countries, antibiotics are unregulated and available as over the counter without any prescription. This lack of regulation results in antibiotics that are easily accessible either available through online in few countries, plentiful, and cheap, which promotes overuse.

Inappropriate prescribed antibiotics also are one of the reasons for the promotion of resistant bacteria. Few Studies have shown that treatment indication, choice of agent, or duration of antibiotic therapy is incorrect in 30% to 50% of cases. In one U.S. study reported that a pathogen was defined in only 7.6% of 17,435 patients hospitalized with community-acquired pneumonia (CAP)¹³. In comparison, investigators at the Institute were able to identify the probable pathogen in 89% of patients with CAP through use of molecular diagnostic techniques(PCR).In addition, 30% to 60% of the antibiotics prescribed in intensive care units (ICUs) have been found to be unnecessary and inappropriate¹⁴.

In few research studies which have been stated that Changes in antibiotic-induced gene expression can increase virulence, while increased mutagenesis and

HGT promote antibiotic resistance and spread. Low levels of antibiotics have been shown to contribute to strain diversification in organisms such as *Pseudomonas aeruginosa*¹⁵. Subinhibitory concentrations of piperacillin and/or tazobactam have also been shown to induce broad proteomic alterations in *Bacteroides fragilis*.

Extensive Agricultural Use is common worldwide in both developed and developing countries, antibiotics are widely used as growth and nutritional supplements in livestock¹⁶. The antibiotics used in livestock are ingested by humans when they consume food. The transfer of resistant bacteria to humans by farm animals was first noted more than 35 years ago, when high rates of antibiotic resistance were found in the intestinal flora of both farm animals and farmers. The sequence of events which occurs is as follows first the antibiotic use in food-producing animals kills or suppresses susceptible bacteria, allowing antibiotic-resistant bacteria to thrive then from them the resistant bacteria are transmitted to humans through the food which we consume and later on these bacteria cause infections in humans which may lead to adverse health consequences¹⁷.

Antibiotic resistance is becoming a worldwide increasing public issue and also the development of newer drugs at still at research level or for FDA approval¹⁸. Hence the treatment given should be prioritized and used symptomatically which can help the patient to get a better pharmaceutical care. Unfortunately, the growing problem of Gram-negative resistance was not parallel to the discovery of antibiotics to treat caused by these bacteria¹⁹, resulting in a substantial number of untreatable infections. even this antibiotic resistance and uses have to be known to the public while prescribing or issuing the drugs regarding when it has to be used and not to be taken frequently in order to reduce the drug resistance issues in case of life threatening conditions and provide the overall population a better pharmaceutical care when needed²⁰.

CONCLUSION:

According to the data included various articles have been referred and we conclude that Rapidly emerging resistant bacteria threaten the extraordinary health benefits that have been achieved with antibiotics²¹. Each time our world faces a predictable, but an inevitable tragic outcome, the first reaction is to join forces and to bring together all the information, knowledge and tools necessary to get a particular solution. Doctors, pharmacists, scientific researchers and other medical and paramedical staff, the general public should all share the valid information known antimicrobials, infections, resistance and therapy²². Coordinated efforts to implement new policies, renew research efforts, and pursue steps to manage the crisis are greatly needed.

Proper Observation and care is a crucial factor in creating a path to reach the effects caused by resistance. Resistance is a critical public health issue that needs Integration of data which can minimize the world wide health issues and may also help in newer development of drugs and effective therapeutically and we need to think globally and a particular research should be useful to the overall population²³.

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