ejpmr, 2020,7(3), 250-254

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Review Article

ISSN 2394-3211

EJPMR

ANTIBIOTIC RESISTANCE: GLOBAL THREAT TO PUBLIC HEALTH

***Kasekar N. M., Hajare F. P., Jadhav K. V., Kadam V. J.**

C.B.D. Belapur Maharashtra India.

***Corresponding Author: Kasekar N. M.**

C.B.D. Belapur Maharashtra India.

Article Received on 29/12/2019 **Article Revised on 19/01/2020** **Article Accepted on 09/02/2020**

ABSTRACT

Antibiotics are a type of antimicrobials used in the treatment and prevention of bacterial infections in human and in animals. Infections from resistant bacteria are now universal, and some pathogens have even become resistant to multiple types or classes of antibiotics. The loss of effective antibiotics declines the ability to fight infectious diseases and manage the infectious complications. Bacteria, not humans or animals, become antibiotic-resistant. These bacteria could infect humans and animals, and therefore the infections they cause are more durable to treat than those caused by passive resistor bacteria. The matter of antibiotic resistance may be reduced solely by concerted efforts of all members of society for guaranteeing the continued potency of antibiotics. Wherever antibiotics may be bought for human or animal use without a prescription, the emergence and unfold of resistance is created worse. Similarly, in countries without standard treatment tips antibiotics are typically over-prescribed by medical examiners and veterinarians and over-used by the general public. A worldwide and interdisciplinary approach should be considered for the development of recent screening and diagnostic tools. This review article focuses on prevention of antibiotic resistance, its safe use, its mechanism and its global awareness. It is mainly concerned with resistance of antibiotic which is becoming a global threat to public health.

KEYWORDS: Antibiotics, resistance, efficiency, guidelines, global awareness.

INTRODUCTION[1,2,3,4,5,6]

Antibiotics are the 'wonder drugs' to combat microbes. For many years, multiple varieties of antibiotics haven't solely been used for therapeutic functions however practiced prophylactically across different industries such as agriculture and animal husbandry. Uncertainty has arisen, as microbes became proof against common antibiotics whereas the host remains unaware that antibiotic resistance has emerged. Antibiotics either are cytotoxic or cytostatic to the micro-organisms, permitting the body's natural defenses, like the immune system, to eliminate them. They typically act by inhibiting the synthesis of a microorganism cell, synthesis of proteins, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), by a membrane disorganizing agent, or different specific actions. To combat against infections or microbes, without doubt antibiotics are a blessing to human civilization that has saved voluminous individuals. Antibiotic treatment is one amongst the most approaches of recent drugs that is used to combat infections. The "golden era" of antibiotics ranged from the 30s to 1960s that gave rise to several antibiotics. Unfortunately, these eras finished as a result of researchers were unable to take care of the pace of antibiotic discovery within the face of rising resistant pathogens. Persistent failure to discover new antibiotics and no judicious use of antibiotics are the precursors related to the emergence of antibiotic resistance. Antimicrobial resistance (AMR) poses a heavy international threat of growing concern to human, animal and setting health.

Types of resistance[7]

1) Intrinsic Resistance

Whereby microorganisms naturally don't possess target sites for the medicine and so the drug doesn't have an effect on them or they naturally have low permeableness to those agents as a result of the variations within the chemical nature of the drug and therefore the microbial membrane structures especially for those who need entry into the microbial cell in order to affect their action. With intrinsic resistance the organism possesses properties that build it naturally resistant to bound insults, e.g. the more complex outer layer of gram negative bacteria makes it far more tough for certain antimicrobials to penetrate.

A good analogy in individuals is sun tolerance; darker individuals' people have a higher melanin content within the skin that produces them more tolerant of the sun's harsh rays than people with fair skin. This can be intrinsic resistance to the sun's rays built up by millennia of genetic choice in hot countries. Thus intrinsic resistance is considered to be a natural and heritable property with high predictability. Once the identity of the organism is known, the aspects of its anti-microbial resistance are recognized.

2) Acquired Resistance

Acquired resistance is once a naturally prone organism acquires ways of not being affected by the drug. Any insult, physical or chemical, has the potential to induce changes in the organism. Again our sun tolerance analogy shows us the fair skinned people, by gradual exposure, (sun tanning) can become more sun tolerant. Microbes are more ubiquitous however, and can actually acquire resistance from each other by sharing genetic material. They can pass genetic material from one to another in various ways; thus microbes have been performing their own genetic modification for millions of years.

This is known as horizontal gene transfer (HGT) and can be a much more rapid process than the genetic selection required for intrinsic resistance. In addition, while our sun tan analogy simply requires more melanin accumulating in skin cells, microbes have several mechanisms they can resort to in order to develop resistance.

Mechanism of resistance[8,9,10,11]

1. Decreased Uptake

Gram positive bacteria have a plasma membrane composed largely of peptidoglycan, a very rigid substance. This is often a prime target of β lactam antimicrobials like penicillin and cephalosporins. The antimicrobial locks on to the β lactam structure within the plasma membrane, preventing enlargement, and also the cell ruptures as it grows.

Gram negative bacteria have a way much thinner plasma membrane itself and this is protected by a lipopolysaccharide molecule within the capsule, an associate outer membrane and what's called the periplasmic area. Briefly it's a way additional heavily armored vehicle.

Porins are openings within the protoplasmic membrane through that antimicrobial agents will gain entry, a reduced range of such porins is one suggests that of antimicrobial resistance.

2. Mutation

When an antimicrobial attacks a particular target, whether it is cell membrane peptides, ribosomes or nuclear DNA, it locks on to specific receptors on the target. Bacterial mutation leads to the alteration of those receptors in order that the antimicrobial can no longer fit and the organism so immune to the effects of the antimicrobial.

3. Enzyme inactivation

Some microorganisms have developed the ability to produce enzymes that are able to inactivate certain antimicrobials. The most notable example is penicillinase that can inactivate penicillin, but there are others. Clavulanic acid can bind penicillinase leaving the antimicrobial amoxicillin to do its work, and also there are the penicillinase resistant penicillins such as methicillin and cloxacillin, but they are still subject to target alterations (see below) making them ineffective over time.

4. Efflux Pumps

Some bacteria, e.g. Pseudomonas, have a system called an efflux pump. As its name suggests this is a system whereby the bacterium has a pump to expel ingested chemicals. Although a number of these drug efflux pumps transport specific substrates, many are transporters of multiple substrates.

The design of specific, potent efflux pump inhibitors appears to be a crucial goal for the improved control of infectious diseases within the near future. For instance, in ear therapy tris-EDTA has the potential to partially inactivate the efflux pump but this is often only a topical specified action not generally available in most situations.

5. Biofilms

Biofilms are complicated microorganisms communities containing microorganism and fungi. The microorganisms synthesize and secrete a protecting matrix that attaches the biofilm firmly to a living or non-living surface. At the foremost basic level a biofilm may be delineated as bacteria embedded in a very thick, slippy barrier of sugars and proteins. Biofilms have long been known to be created on surfaces of medical devices, like urinary catheters, endotracheal and tympanostomy tubes, orthopedic and breast implants, contact lenses, intrauterine devices (IUDs) and sutures. They are a significant contributor to diseases that are characterized by an underlying bacterial infection and chronic inflammation, e.g. periodontitis, cystic fibrosis, chronic acne and osteomyelitis Biofilms are also found in wounds and are suspected to delay healing in some. Planktonic bacteria attach within minutes and form strongly attached small colonies within 2–4 hours. They become progressively tolerant to biocides, e.g. antimicrobials, antiseptics and disinfectants, within 6–12 hours and evolve into absolutely mature biofilm colonies that are extraordinarily proved against resistant to biocides and shed Planktonic bacteria within 2–4 days, depending on the species and growth conditions. They quickly recover from mechanical disruption and reform mature biofilm within 24 hours. A unique property of polymicrobial biofilms is that the cooperative protective effects that different species of micro organism will give to every alternative.

Horizontal Gene Transfer – The Gist[12]

1) Horizontal gene transfer (HGT) is a vital mechanism for the growth of antibiotic resistance.
2) HGT is faster than simple mutation.
3) HGT is carried by three mechanisms.

a. Transformation

Transformation refers to the ability of microorganisms to utilize snippets of free DNA from their surroundings. DNA from dead cells gets shed into fragments and exits the cell. The free-floating DNA will then be picked up by competent cells. Exogenous DNA is taken up into the recipient cell from its surroundings through the cytomembrane. The exogenous DNA is incorporated into the host cell's chromosome via recombination. Transformation leads to genetic alteration of the recipient cell.

b. Transduction

Transduction is the process by which viruses that prey upon bacteria, known as bacteriophage, can transmit genetic material from one organism to another. It is similar to the way mosquitoes transmit disease from animal to animal. However, while the mosquito is a passive carrier, bacteriophage are more complicated.

Being viruses themselves they inject their genetic material into a bacterial cell and replicate there to a great degree. Their traditional mode of replica is to harness the replicational, transcriptional, and translation machinery of the host micro organism to create various virions, or complete infectious agent, as well as the viral DNA or RNA and the supermolecule protein coat. The packaging of virus DNA has low fidelity and little pieces of microorganism DNA, along with the bacteriophage genome, could become packaged into the bacteriophage genome. At the same time, some bacteriophage genes are left behind within the microorganism body.

When the cell eventually ruptures it emits many more bacteriophage into the surroundings to infect other microorganisms.

c. Conjugation

Bacterial conjugation is that transfer of genetic material between microorganism's cells by direct cell-to-cell contact or by a bridge-like affiliation between two cells. It's a mechanism of horizontal gene transfer as area unit transformation and transduction though these two different mechanisms don't involve cell-to-cell contact.

Bacterial conjugation is usually considered as the bacterial equivalent of reproduction or mating since it involves the exchange of genetic material. During conjugation the donor cell provides a conjugative or mobilizable genetic element that is most often a plasmid or transposons.

4) Conjugation is crucial means of HGT
5) Integrons contain the fundamental genetic material and that they are picked up by transposons that insert them into plasmids or chromosomes
6) Plasmids could also be shared with totally different bacterial species which means that commensals (non-target organisms) are necessary within the spread of AMR.
7) Integrons usually carry resistance genes to more than one antimicrobial, leading to co-selection for resistance to many antimicrobials at just one occasion.

Superbugs

The word "superbugs" denotes microbes with higher morbidity and elevated mortality rate due to many mutations providing resistance to numerous categories of antibiotics. Therapeutic preferences for these resistant microbes are less, and these are related to a prolonged stay at hospital and increased economic value. Due to aberrant use of antibiotics, various bacterial human pathogens have evolved into MDR varieties. Mycobacterium tuberculosis may be a distinguished example from each of the developing and the developed world. S. aureus is taken into account because the most ill famed superbug. It's a nasal commensal of humans and might cause common skin infections.

Spread of Resistance[13,14,15]

Spread of both resistant bacteria and the potential for horizontal gene transfer means that resistance can spread rapidly not only within a population but to a wider arena. The close interplay between humans, animals and their environment can be seen in this graphic. This led to the formation of the One Health approach to antimicrobial resistance whereby humans, animals and the environment are all taken into consideration when dealing with issues of antimicrobial resistance; concentrating on only one sector will not be very successful and control of all must be co-ordinate to be effective. The interplay between humans and animals is well documented. The risk of resistance developing in food animals and resistant organisms being transferred to humans by other close animal contact or via the table is real enough but hygiene; either at slaughter or food preparation, and cooking can dramatically reduce this risk. There is also the very close contact between many people and their pets that can result in resistance transfer; this can be pet to human or the other way, human to pet. The environment is vitally important; we are all part of it, humans and animals. In addition it is clear that the resistance risk is much higher where there are concentrated populations, such as in hospitals and intense animal rearing situation. Antimicrobial use is higher in monogastric species (poultry and pigs), compared to other food producing animals. Use is much lower in the extensive pasture based farming systems that predominate in New Zealand. The high amount of air travel in the human population can disseminate resistant infections and also breeding stock importation can propose a great risk. The latter may be mitigated in the future by using semen transport instead of live animals.

Global scenario[16]

The Centers for Disease Control and Prevention (CDC) estimates quite two million people are infected with antibiotic-resistant organisms, leading to around 23,000

deaths annually within the U.S, cost accounting $20-$35 billion annually.

In Europe

- An estimated 25,000 deaths are because of antibiotic-resistant infections, costing €1.5 billion annually.

In India

- It is calculated that 58,000 neonatal infection deaths are owing to drug resistant Infections.
- The countries consuming the foremost antibiotics overall in 2010 were India, 13 billion SU; China, 10 billion SU; and therefore the U.S 7 billion SU.
- In per capita terms among these countries, the U.S led in 2010 with 22 SU per person, compared with 11 SU in India and 7 SU in China.
- W.H.O 2014 reported that according E. coli resistance of more than 50% fluoroquinolones and third generation cephalosporins.
- K.pneumoniae resistance rates to third generation cephalosporins exceed 30- 60%. MRSA resistance rates exceed 20-80%.

Between 2000 and 2010, total international antibiotic consumption grew by over 30 percent, from just about 50 billion to 70 billion standard units.

In most countries, about 20 percent of antibiotics are employed in hospitals and other healthcare facilities, and 80 percent are employed in the communities, either prescribed by healthcare providers or purchased directly by customers or caregivers without prescription.

Causes[17]

1. Inappropriate usage & misuse of antibiotics.
2. Indiscriminate use of antibiotics in agricultural and veterinary practice.
3. Lean research and development.

Inappropriate use of antibiotics[15]

- The insufficient prescription of antibiotics for viral infections.
- Frequent prescription of "broad-spectrum antibiotics", rather than higher targeted antibiotic.
- Patient failure to stick to regimens for prescribed antibiotics.

Initiatives taken by India[17]

1. The National Policy for Containment of the Antimicrobial Resistance.
2. National Anti-Microbial Resistance Research and Police investigation network.
3. Jaipur declaration (a WHO initiative).
4. Chennai city declaration.
5. The Drugs and Cosmetic Rule, 1945 were amended in 2013 to incorporate a new Schedule H1.
6. National Treatment Guidelines for Antibiotic Use in Infectious Diseases.

How to tackle resistance[17]

1. People

- ✓ Utilization of antibiotics, prescribed by a doctor.
- ✓ Completing the entire antibiotic course, though they feel better.
- ✓ Not sharing antibiotics with others or mistreatment of leftover prescriptions.
- ✓ Educating the public by awareness.
- ✓ Stopping the utilization of antibiotics as growth-promoters in stock.

2. Doctors and pharmacists

- ✓ Enhancing infection prevention and management.
- ✓ Prescribing and dispensing antibiotics only if they're actually required, after antibiotic sensitivity testing, once possible.
- ✓ Prescribing and dispensing the proper antibiotics to treat the illness.
- ✓ Ban on OTC sale of antibiotics.
- ✓ Complying the rules and regulations.

3. Policymakers

- ✓ Having national plans and tips on antimicrobial resistance.
- ✓ Strengthening resistance trailing and laboratory capability.
- ✓ Regulating and promoting applicable use of medicines.
- ✓ Increase defrayment on innovation and infrastructure.

4. Industry

- ✓ Promoting innovation and research and development of latest tools.
- ✓ Promoting Cooperation and Knowledge Sharing Among all Stakeholders.

CONCLUSION

We should get to extend our data relating to the extent of the antibiotic resistance issue. Majority of people aren't responsive to antibiotic resistance, its mechanism, its causes and its prevention. Current international interest indicates that AMR isn't an unheeded issue any longer. Antibiotic resistance has been found altogether regions of the globe. Modern travel of individuals, animals, and goods means antibiotic resistance will simply spread across borders and continents. Cooperative, coordinated efforts can help slow the development and spread of antibiotic resistance and shield individuals. For example, implementing prescriptions only laws and eliminating over-the-counter antibiotic purchases could cut off antibiotic purchases for few segments of the population, like the rural poor. At the national, regional, and international levels, the tracking, bio-surveillance, and response and prevention methods of AMR, pathogens could facilitate to manage the "global resistome."

REFERENCES

1. Sojib Bin Zaman, Muhammed Awlad Hussain, Rachel Nye, Varshil Mehta, Kazi Taib Mamun, and

Naznin Hossain, A Review on Antibiotic Resistance: Alarm Bells are Ringing, Cureus, 2017 Jun 28; 1.
2. Levy SB, Marshall B. Antibacterial resistance worldwide: causes, challenges and responses Nat Med., 2004; 10: 122–129.
3. Levy SB. The Antibiotic Paradox: From tragedy the antibiotic age is born Springer, 1992; 1–12.
4. Nathan C, Cars O. Antibiotic resistance-problems, progress, and prospects. N Engl J Med., 2014; 371(19): 1761–1763.
5. Nathan C. Antibiotics at the crossroads. Nature, 2004; 431(7011): 899–902.
6. Davies J, Davies D. Origins and evolution of antibiotic resistance. Microbial Mol Biol Rev., 2010; 74(3): 417–433.
7. Brauner, Fridman, Gefen and Balaban. Distinguishing between resistance, tolerance and persistence to antibiotic treatment. Perspectives May 2016 Volume 14.
8. Bambeke, Balzi and Tulkens. Antibiotic Efflux Pumps. Biochemical Pharmacology, 2000; 60: 457–470.
9. Webber and Piddock. The importance of efflux pumps in bacterial antibiotic resistance. Journal of Antimicrobial Chemotherapy, 2003; 51: 9–11.
10. Phillips PL, Wolcott RD, Fletcher J, Schultz GS. Biofilms Made Easy. Wounds International, 2010; 1(3).
11. Soto. Role of efflux pumps in the antibiotic resistance of bacteria embedded in a biofilm. Virulence, April 1, 2013; 4:3, 223–229.
12. Dennis Scott, The mechanics of antibiotic resistance, March 2017.
13. Cantón and Morosini. Emergence and spread of antibiotic resistance following exposure to antibiotics FEMS Microbiological Revue, 2011; 35: 977–991.
14. McEwen and Fedorka-Cray. Antimicrobial Use and Resistance in Animals. Clinical Infectious Diseases, 2002; 34(Suppl 3): S93–106.
15. Wall, Mateus, Marshall, Pfeiffer, Lubroth, Ormel, Otto and Patriarchi. Drivers, Dynamics and Epidemiology of Antimicrobial Resistance in Animal Production. FAO 2016.
16. Global action plan on antimicrobial resistance 2015.pdf
17. PT. B.D.SHARMA, PGIMS, ROHTAK, ppt.