Combating antibiotic resistance: a major challenge

Leena Sawaikar, Celina Nazareth*, Swati Keny

PES's Rajaram and Tarabai Bandekar College of Pharmacy, Farmagudi, Ponda, Goa, India - 403401.
celinanaz@yahoo.com

1.Introduction

Antibiotics are microbial metabolites or synthetic analogues inspired by them that in small doses inhibit the growth and survival of microorganisms without serious toxicity to the host (1). These drugs have revolutionized medicine and made our modern way of life possible. Antibiotics target and inhibit essential cellular processes, retarding growth and causing cell death. Antibiotics are essential for preventing and treating infectious diseases (2). From the time of discovery of the first antibiotic, the challenge of antibiotic resistance commenced. Antibiotics use different mechanisms against bacteria to prevent their pathogenesis and they can be classified as bactericidal or bacteriostatic. At the same time, bacteria are also using methods to overcome the effectivity of the antibiotics by using distinct types of mechanisms. This ability of microorganisms to survive and be viable under the influence of antimicrobial agents is called as antibiotic resistance (3). Knowing the mechanism by which the organisms develop this resistance helps to overcome the resistance and also to formulate synthetic antimicrobials to overcome the current mechanism of resistance. However, if bacteria are exposed to drugs below the dose required to kill all bacteria in a population (the minimum bactericidal concentration or MBC), they can mutate and resist antibiotic treatment via natural selection for resistance-conferring mutations. These genetic mutations can arise from the adoption of a plasmid encoding a resistance gene or by mutation to the bacterial chromosome itself.

2.Mechanism of resistance

A common mechanism used by bacteria to minimize the effects of antibiotics is to acquire or increase the expression of drug efflux pumps. Bacteria use pumps in the cell wall to expel the antibiotic. And these pumps expel drugs from the cytoplasm, limiting their ability to access their target (4).

Enzymatic inactivation: An existing bacterial enzyme is modified to interact with an antibiotic in order to make them inactive towards bacteria. It is due to the transfer of the antibiotic resistance gene carried on plasmids. The most significant examples are beta-lactamase enzymes, which hydrolyse beta-lactams (penicillins, cephalosporins).

Decreased uptake by changes in the outer membrane permeability or by presence of porins: These variations interfere with the entrance of antibiotics.
Modification of the drug target: These changes impede the binding of the antibiotic and limit its potency (5).

3.Clinical causes of antibiotic resistance (6)

The main origin of resistance to antibiotics is their misuse. An example is unnecessary prescription of antibiotics for viral infections, against which they are ineffective.
In most of the low income countries most of the antibiotics are of secondary quality and available over the counter. Wherever there is insufficient enforcement of regulatory policies on prescribing medicine, over-the-counter antibiotics are prevalent. Such availability makes it accessible for patients to do self-treatment for diseases that do not necessarily need antibiotics for treatment.

Antibiotic resistance can develop because physicians unnecessarily prescribe lengthy courses of antibiotics. Another factor contributing to overprescribing antibiotics by providers is patient's expectations from the clinicians. It is seen that clinicians consider the perceived patient request for antibiotics as one of the major barriers to adhere to standard guidelines for antibiotic prescriptions and hence to avoid the dissatisfaction of their patients prescribe antibiotics.

The usage of antibiotics in agriculture is one of the significant factors in developing antimicrobial resistance in humans. Antibiotics are added to animal feed and drinking water to cure sick animals and to prevent illness (prophylaxis) in healthy animals and in animal farming worldwide to promote the growth of livestock, particularly colistin, a critical last-line antibiotic to treat severe infections in humans (7).

Inappropriate prescribing patterns which include prescription of broad spectrum antibiotics in place of a better targeted antibiotic.

Improper use by the patient with respect to dosage or duration of the treatment which makes some of the bacteria survive and become resistant.
Development of superbugs which can adapt to the medicines that are intended to kill them and fight back against them. These multiply and cause infections despite treatment with different antibiotics. Some infections with superbugs include gonorrhoea, MRSA and tuberculosis (8).

4. Consequences of antibiotic resistance

Infections caused by resistant bacterial strains can cause more severe infections which may be fatal or difficult to treat as compared with similar infections caused by susceptible strains. Antibiotic resistant infections cause economic and health burden to the nation. When first-line and then second-line antibiotic treatment fail, more antibiotics which are more toxic and expensive have to be administered. Patients with resistant infections require significantly longer hospital stays, more doctor's visits, and may experience a higher incidence of long-term disability (9).

Finally when antibiotics don't work, it can lead to

- Illnesses lasting for a longer time with complications.
- Frequents visits to the doctor
- Usage of more potent and expensive medications
- Increased bacterial infection related mortality.

5.Bacteria resistant to antibiotics (10)

Antibiotics which were earlier used to treat a particular infection have become ineffective against a particular bacteria. The development of bacterial resistance by some strains of bacteria to most of the easily available antibiotic has created a major issue in the field of medicine. Methicillin-resistant Staphylococcus aureus (MRSA), vancomycin-resistant Enterococcus (VRE), multi-drug-resistant Mycobacterium tuberculosis (MDR-TB) and carbapenem-resistant Enterobacteriaceae (CRE) gut bacteria are some of these which causes serious disease and a major public health problem.

6. Strategies to combat antibiotic resistance (11)

6.1. Measures to be taken by the patients

Medications should be taken as per the doctor's prescription the medication as prescribed by your doctor. Treatment should not be stopped even if the patient is feeling better. If the treatment is stopped soon, the patient may fall sick again and bacteria may become resistant to the antibiotic taken.

No skipping of dose is allowed as the medicine is effective only if the blood levels of the same are maintained.

An antibiotic is meant for a particular infection at the time, hence using the leftover antibiotic is not appropriate. By taking the incorrect medication, receiving the right care on time is delayed and thus the illness gets worse.

Antibiotics prescribed for someone else should not be taken as these may not be appropriate for your illness so this can delay or worsen the treatment. If any new or unusual symptoms or side effects are observed it should be informed to the physician so that the trouble causing antibiotic can be stopped and the treatment be completed with a different antibiotic (12-13).

6.2.Measures to be taken by physicians

Prescribing a short-course antibiotic therapy: Recent randomized controlled trials show that shorter courses of antibiotic therapy are as effective as longer courses, with the added benefit of reducing the exposure of patients to antibiotics. This is because most of the signs and symptoms of bacterial infections result from the inflammatory response to the bacteria rather than the direct presence of viable bacteria (14).

Antibiotic stewardship programmes have to be conducted. These ensure that each patient is given best care for their specific condition and gets an antibiotic only when necessary. Effective sanitation, hygiene and infection prevention measures ensure that incidence of infection is reduced. Clinical guidelines to be followed. Use delayed antibiotic prescriptions (15-16).

6.3. National strategies (17)

Establishment of national committee to monitor impact of antibiotic resistance and provide intersectoral co-ordination is required. Establishing and implementing national standard treatment guidelines, having essential drug list (EDL), enhancing coverage of immunization are other essential strategies desired at national level. A national policy for containment of antimicrobial resistance (AMR) was introduced in 2011. The policy aims to understand emergence, spread and factors influencing resistance, to setup antimicrobial program, to rationalize the use of antimicrobials and to encourage the innovation of newer effective antimicrobials. Other than this, it also aims establishing antibiotic resistance surveillance system, strengthening infection prevention and control measures and educate, train and motivate all stake holders in rational use of antibiotics.

7.Conclusion

Antibiotic resistance is a serious issue with a wide range of causes. It is major cause of health concerns adding cost to oneself and to the community, directly or indirectly. The best way to combat it is prevention so that the spread of infection is reduced. The need of the hour is to develop newer antibiotics and sensible usage of presently available antibiotics. To combat the globally growing antibiotic resistance, patients, prescribers, and individuals must work together with international regulators and policy makers.

References

1. Williams DA, Foye WO, Lemke TL. Foye's principles of medicinal chemistry. 5th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 2002.
2. Habboush Y, Guzman N. Antibiotic Resistance. StatPearls Treasure Island. 2022.
3. Abushaheen MA, Muzaheed, Fatani AJ, Alosaimi M, Mansy W, et al. Antimicrobial resistance, mechanisms and its clinical significance. Dis Mon. 2020;66(6):100971.
4. Richardson LA. Understanding and overcoming antibiotic resistance. PLoS Biol. 2017 Aug 23;15(8):e2003775.
5. Annunziato. Strategies to overcome antimicrobial resistance making use of non-essential target inhibitors: A review. International Journal of Molecular Sciences. 2019:20(23):5844.
6. Aslam B, Wang W, Arshad MI, Khurshid M, Muzammil S, Rasool MH. Antibiotic resistance: a Rundown of a Global Crisis. Infection and Drug Resistance. 2018;11(11):1645-58.
7.Antibiotic Resistance: What Is It, Complications & Treatment. Cleveland Clinic; 2021. Available from: https://my.clevelandclinic.org/health/articles/21655-antibiotic-resistance
8. Dadgostar P. Antimicrobial resistance: Implications and costs. Infect Drug Resist. 2019;12:3903-10.
9. Sifri Z, Chokshi A, Cennimo D, Horng H. Global contributors to antibiotic resistance. Journal of Global Infectious Disease. 2019:11(1):36.
10. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. Pharmacy and therapeutics.2015;40(4):277–83.
11.Antibiotic resistant bacteria [Internet]. Gov.au. [cited 2023 Aug 2]. Available from: https://www.betterhealth.vic.gov.au/health/conditionsandtreatments/antibiotic-resistant-bacteria
12. Wall S. Prevention of antibiotic resistance - an epidemiological scoping review to identify research categories and knowledge gaps. Glob Health Action. 2019 [cited 2023 Aug 2];12(1):1756191. Available from: http://dx.doi.org/10.1080/16549716.2020.1756191
13. Combating antibiotic resistance [Internet]. U.S. Food and Drug Administration. FDA; 2020 [cited 2023 Aug 2]. Available from: https://www.fda.gov/consumers/consumer-updates/combating-antibiotic-resistance
14. Nathan C. Resisting antimicrobial resistance. Nature Reviews Microbiology. 2020;18(5):259-60.
15. Spellberg B. The maturing antibiotic mantra: "shorter is still better." Journal of Hospital Medicine. 2018;13(5):361-2.
16. Fda.gov. [cited 2023 Aug 2]. Available from: https://www.fda.gov/consumers/consumer-updates/combating-antibiotic-resistance.
17. Nfid.org. [cited 2023 Aug 2]. Available from: https://www.nfid.org/antibiotic-resistance/antibiotic-stewardship-pledg