Imperial Journal of Interdisciplinary Research (IJIR)
Vol-2, Issue-7, 2016
ISSN: 2454-1362, http://www.onlinejournal.in

Antimicrobial Resistance: A Global Threat

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Abstract: *Easy availability of the antimicrobial drugs leading to their misuse by all, poses the major problem of amr in last two decades all over the world –becoming a critical health issue today. In recent years the emergence of resistance to reserve drugs was particularly come into notice. Cross resistance to various drugs is another major threat.To combat with this problem efforts to be put through all including government, health policy makers, doctors, health care workers. Who is managing amr by guiding through: policy guidance, support for surveillance, knowledge generation and partnerships, including through disease prevention and control programs; essential medicine quality; infection prevention and control; patient safety; and laboratory quality assurance. Cooperation between the medical personal, regulating agencies and pharmaceutical industry will be needed to define policies checking the sale of antimicrobial drugs, public education program regarding the hazards of inappropriate antibiotic use.*

Keywords*: antimicrobial resistance, antibiotics*

Introduction

With introduction of antibiotics against infection caused by microorganisms, premature death due to infection would become history. Ungenerous use of antimicrobial drugs leads to development of drug resistance organism. Antimicrobial resistance is not a new phenomenon; but the speed with which the new resistance phenotypes have emerged poses a great threat to antimicrobial use.(1)(2)

Resistance rates for many isolates are rising but are highly different. For example, the isolates of Staphylcoccusaureus resistant to methicillin increased from zero in 10–17 years ago to approximately 70% in Japan , 40% in Belgium, 30% in the United Kingdom, and 28% in the USA by 1998 (1). Recent rates of resistance to Streptococcus pneumoniae were less than 2% in Belgium, Italy, and Finland, but7%in Germany, 9.5% in Iceland, 44% in Spain and 58% in Hungary. (3)

Increasing antimicrobial resistance (AMR) presents a major threat to public health because it leads increase in morbidity, death and economic burden.(4) For example, the mortality rate in resistant strains of Salmonella spp. was found to be 3.4%, whereas it was only 0.2% in those involving sensitive strains (5). In 1995 the cost of containing an outbreak of infection caused by methicillin-resistant S. aureus in a district general hospital in the United Kingdom was estimated to exceed US$ 560 000 (6).

Reasons For The Emergence Of Resistance

The reasons for resistance are many and are related to antimicrobial use, availability of the appropriate host and complex biochemical/ genetic mechanisms either newly acquired by the microbes or those simply being 'turned on' as the need arises, i.e. on exposure to antimicrobials.7-12

Inappropriate use of antibiotics

The excessive use and misuse of antimicrobial drugs leads to increase in development of antimicrobial resistance. (13). The factors responsible include over-the-counter availability of antimicrobials without professional controls (14), the use of drugs of low potency and effectiveness as a result of poor manufacture (15) or counterfeiting (16), and the availability of drugs from roadside stalls and hawkers without knowledge of dosage regimens, indications or contraindications (17). Containment of AMR thus requires a range of strategies. AMR is a global problem (18). Globalization increases the vulnerability of countries to imported diseases, and infectious diseases spread throughout. (19-20).

Combination of one or more antimicrobial drugs for treatment and prevention of infection of the immune compromised host, e.g. patients with malignancy , patients following solid organ or bone marrow transplant, Similarly, with the advent of

intensive care units, trauma centers and bum care units extending the life of critically ill patients on multiple antibiotics, responsible for the development of resistance to antimicrobials. The increase in hospital stay of compromised patients also resulted in an increase in the nosocomial infection rate by drug-resistant bacteria.2-4-6

Low socio economic status and overcrowding

Increase in poverty, overcrowded living areas, crowded day care centers and lack of education have contributed to the spread of bacteria. Lack of adequate hand-washing by all health care workers, particularly physicians, remains a universal problem. They all causes infection leading to excessive use of antibiotics, responsible for antimicrobial drug resistance. Lack of medical services to the poor and mentally incompetent who may be at the greatest risk of receiving as well as spreading infection.

Global Nature of The Problem

Scientific literature over the past decade has testified to the global nature of the problem.21-22-23 Resistant *Streptococcus pneumonia* isolates were first reported in the 1960s fol1owing the extensive use of tetracycline. *Streptococcus pneumoniae*isolates, highly resistant to penicillin, were first isolated from miners in Durban, South Africa in 1977.24 Penicillin and multidrug-resistant *Streptococcuspneumoniae*isolates have now been documented from all parts of the world; the percentage of resistant isolates is particularly high from various countries in Europe, South America and South-east Asia. So the resistant strains of bacteria become prevalent all over the world. Thus the global nature of the problem requires the global response.

Mechanisms Of Antibiotic Resistance

Various mechanisms by which microorganisms exhibit resistance to antimicrobials are:

1. Drug inactivation or modification: in this type of resistance bacteria develops enzymes against antibiotics rendering it inactive. for example, enzymatic inactivation of *penicillin* G in penicillin-resistant bacteria through the formation of β-lactamases. The protective enzymes produced by the bacterial cell will attach an acetyl or phosphate group to a specific site on the antibiotic, which will reduce its ability to bind to the bacterial ribosomes and inhibit protein synthesis.[25]
2. Alteration of target site: in this type drugs is not able to bind its target site due to alteration in binbing proteins. for example, alteration of protein binding site of penicillins—in MRSA and other penicillin-resistant bacteria. Another protective mechanism found among bacteria is ribosomal protection proteins. These proteins protect the bacterial cell from antibiotics that attack the cell's ribosomes to inhibit protein synthesis. The ribosomal protection proteins binds to the ribosomes of the bacterial cell, which causes conformational changes in it. This allows the ribosomes to synthesize proteins essential to the bacteria while preventing antibiotics from binding to the ribosome to inhibit protein synthesis.
3. Alteration of metabolic pathway: In this mechanism bacteria acquire some alternative metabolic pathway to perform the functions. for example, some sulfonamide-resistant bacteria do not require para-aminobenzoic acid (PABA), a precursor for the synthesis of folic acid or nucleic acids in bacteria inhibited by sulfonamides. Whereas humans require preformed folic acid.26
4. Reduced drug accumulation: in this method bacteria decreases drug permeability or increases active efflux (pumping out) of the drugs across the cell surface. These specialized pumps can be found in the cellular membrane of certain bacteria to pump antibiotics out of the cell before they are able to cause any damage.27

Two basic mechanism –either Bacteria may acquire mutations that inhibits antimicrobial agents to reach the intracellular target site by down regulation of porin genes, thus the susceptible bacteria may become resistant to antimicrobial agents through mutation and selection, or by acquiring the genetic information from the resistant bacteria that encodes resistance. The transfer of genetic material can occur by transformation, conjugation, or transduction. through genetic exchange method, bacteria may become resistant to many antibacterial agents, and these bacteria with multidrug resistance (defined as resistance to ≥3 antibacterial drug) become cause of concern, in hospitals and healthcare institutions where they occur most commonly.

Acquired resistance that develops due to chromosomal mutation is called *vertical evolution.*susceptible bacteria can become resistance to an antibiotic through new mutations.[28] strains of bacteria carrying resistance-confers mutations are selected by antimicrobial use, it kills the susceptible strains but allows the newly resistant strains to survive and grow.

Horizontal evolution means bacteria develops resistance through acquiring the new genetic material from other resistant bacteria. This can be in strains of same species or different species or genera. Basic mechanism for genetic exchange is transduction, conjugation and transformation.[28]this transmission occurs through plasmids.

Why is resistance a concern?

Why is antimicrobial resistance becomes a concern globally. Lots of reasons, firstly, resistant bacteria like *Pseudomonas* , staphylococcus, enterococcus, kiebsiellaare becoming common in healthcare institutions. Secondly,Bacterial resistance results in treatment failure, which can cause serious consequences in critically ill patients. Thirdly , it increasing mortality rates in patients with blood infections due to pseudomonas , coagulase-negative staphylococci, enterococci *Staphylococcus aureus*, *K pneumoniae*, 29-30Prolonged therapy with antimicrobial agents, such as vancomycin or linezolid, may also lead to low-level resistance that compromises therapy, but may not be detected by routine susceptibility test used in hospital laboratories.[31]

Resistant bacteria become major infection-control problems, not only in hospitals but in communities also. Infected individuals, including children, often lack identifiable risk factors for MRSA, and appear to have acquired their infections in a variety of community settings32-33 Community-associated MRSA strains are typically less resistant to antimicrobial agents than healthcare-associated MRSA, but are more likely to produce toxins, such as Panton–Valentine leukocidin[33].Finally, with respect to the cost-containment pressures of today's healthcare environment, antibacterial drug resistance adding more on healthcare costs34although its full economic impact remains to be determined.

To Tackle Antimicrobial Resistance

Whole world has to come forward as one to tackle this problem. First we should collect all relevant data to know the depth and then effective management for the same.

Demographic profile of antimicrobial resistance

We should collect data from all parts of world to know the pattern of antimicrobial resistance. Recently, the Expert Group on Antibiotic Susceptibility Tests (EGASTs) published a multicentre study on antibiotic susceptibility patterns of bacterial isolates from hospitalized patients in India. 17 A continuous surveillance for antibiotic susceptibility patterns of bacteria by microbiology laboratories using standard methods (MIC by tube dilution or E-test) is essential to define the extent of the problem.7,18

Collection of data regarding consumption of antibiotics

Over the counter availability of antibiotics leads to its increase consumption responsible for resistance. Collecting such data is really challenging. For this the cooperation of the pharmaceutical industry in providing data regarding geographical use of variousantibiotics by practitioners and sales by pharmacies is required.

Proper prescription for sale of antibiotics

Control can only be done by controlling the inappropriate sale of antibiotics. For this strict polices to be made by regulating agencies local pharmacist should not allow to sale antibiotics without prescription.

In medical centers and hospitals the physician education regarding the appropriate use of antibiotics, an open dialogue between infectious disease experts/microbiologists and physicians and surgeons. It has been shown that regulating antibiotic use significantly reduces hospital costs as well as the development of resistant bacteria.

To create awareness among general population

Main aim is to educate the people about the rational use of antibiotics. This can be done by consumer oriented programs on television, newspapers, radio, informative advertisement in cinemahalls, distribution of posters/pamphlets. Basic aim to make people aware that antibiotics should be taken only for specific indication.

Long term goal-Prevention of infectious diseases

Prevention is always better than cure will always remains the greatest truth. We should develop effective and inexpensive vaccines and implementing national programs for immunization. The widespread use of the

*Haemophilusinfluenzae*type b (Hib) vaccine in the USA has virtually eliminated Hib infections.3,6,19 Use of the influenza vaccine in the elderly and other high-risk populations significantly reduces complications including secondary bacterial pneumonia. Basic measures to prevent infections like maintaining proper sanitation, safe water supply and general hygiene can do miracle in prevention of infection.

Summary

In nut shell we can say bacteria will develop resistance to the available antimicrobial drugs by either new mutations or the exchange of genetic information. In healthcare institutes and hospitals multidrug resistance bacteria becoming a challenge by complicating treatment, thus increasing morbidity and economic burden. To meet this challenge, proper drug at proper dosage and duration for specific indication should be used. This will also prevent the emergence of multidrug resistant organism. All hospitals should follow strictly the infection guidelines to prevent the emergence of resistant strains. Invention of new antimicrobial drugs with different mechanism of action should be done. Finally wise use of existing drugs, formation of new drugs with different mechanism of action, preventing development of multidrug resistant microorganism, follow strictly infection control guidelines can help in controlling antimicrobial drug resistance.

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