

Overview

Drug resistance: a social perspective

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ABSTRACT:

Drug resistance is a defensive strategy developed by the microorganisms to evade the detrimental effects of antimicrobial agents. Over the years microorganisms have successfully counteracted the action of antimicrobials using both genetic methods such as random mutations, chromosomal or plasmid mediated transfer of genetic information and biochemical mechanisms like decreased permeability of the organism to the drug, inactivation of the inhibitor by enzyme produced by the resistant organism, modification of the properties of the drug receptor site, increased synthesis of an essential metabolite antagonistic for the drug. However, the human governed factors viz. faulty prescriptions, misdiagnosis, self medication, incomplete medication, reservation for antibiotic sensitivity tests, supplementation of antibiotics in cattle feed and toiletries seem to have taught and prompted the microorganisms, the so called miniature industries, to gear up to develop antibiotic resistant mechanisms. As a consequence, multi-drug resistant strains have posed a challenge to the humanity. The costly inputs and hardships of scientists in the laboratories unravel the mysteries and present a valuable product and technologies for human well being. However, the judicious use of the process, product or technology remains the joint responsibility of common masses, technocrats and the government. Thus, our roles to curb the factors that lead to drug resistance need to be given key priority. The approach could shun the burden of scientists and open new and well executed front to fight the nuisance of drug resistance.

Keywords:

Drug resistance, Antimicrobials, Medications.

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INTRODUCTION:

Drug resistance is a defensive mechanism developed by the microorganisms to evade the detrimental effects of antimicrobial agents. Over the years number of microorganisms such as *Staphylococcus* (MRSA and VRSA), *Mycobacterium tuberculosis* (multidrug resistant strains), vancomycin resistant *enterococci*, *Streptococcus pneumoniae*, *H. influenzae*, *Vibrio cholerae*, multidrug resistant *Acinetobacter*, *Pseudomonas*, *Serratia*, *Stenotrophomonas* sp, *Escherichia coli* and *Klebsiellae*, *Shigella*, *Neisseria gonorrhoeae*, *Neisseria meningitidis* have successfully counteracted the action of one or the other antimicrobial (Raghunath, 2008). Microorganisms exhibit genetic, biochemical and phenotypic mechanisms to develop this resistance.

- Mutations give rise to drug resistant mutants with altered susceptibility to the drug (Russell, 2002).
- Chromosomal or plasmid mediated transfer of genetic information pertaining to drug resistance from resistant organisms to the susceptible one. Such transfer is accomplished through conjugation, transformation or transduction (Lacey, 1975; Sheehy, and Novick, 1975; Elwell *et al.*, 1978; Brunton, 1986; Dowson *et al.*, 1989).
- Decreased permeability of the organism to the drug (Aires *et al.*, 1999; Poole, 2001).
- Inactivation of the inhibitor by enzyme produced by the resistant organism (Handsfield, 1982; Aronoff, 1989; Tomasz, 1990).
- Modification of the properties of the drug receptor site (Handwerker and Tomasz, 1986; Jabes *et al.*, 1989).
- Altered metabolic pathway, as shown by sulphonamide resistant bacteria that utilize preformed folic acid and do not require presence of PABA in extracellular fluid (Chakraborty, 1996).
- Loss of enzymes involved in drug activation (Rosolan *et al.*, 2002).
- Biofilm formation: The biofilms have been reported to be less susceptible to antimicrobial agents and has reduced sensitivity to inhibitors, thereby adding to their survival (Jabra-Rizk *et al.*, 2006). The findings have shown delayed penetration of Ciprofloxacin into *Pseudomonas aeruginosa* biofilms (Suci *et al.*, 1994). *E. coli* biofilms exhibited decreased susceptibility to ceftrimide (Evans *et al.*, 1990). Similar reports are available in *Staphylococcus aureus* exposed to tobramycin (DuGuid *et al.*, 1990). The resistance shown by these biofilms in general has been attributed to factors such as poor penetration of antimicrobials, nutrient limitation, accumulation of toxic metabolites and decreased oxygen tension (Tresse *et al.*, 1995).
- Salicylate-Induced antibiotic resistance (Cohen *et al.*, 1993).

Obviously, to be fit for survival, the microorganisms have to learn ways to counteract the effects of their killing agents. However, a number of factors might have tempted and given sufficient room to these miniature industries to devise the mechanisms for evading the detrimental effects of the antimicrobials.

Drug resistance: the tempting factors

The researchers have come up with the conclusive evidence to the reasons that felicitate the organisms to gear up for drug resistance.

- Faulty medical prescriptions: About 50% of the antibiotic prescriptions in the hospitals are given without clear evidence of infection or adequate medical indication (Jain, 1996).
- Misdiagnosis of certain infections have led to wrong administration or unwanted /undue prescription of antibiotics (Willey *et al.*, 2007). Physicians have administered antibacterial drugs to patients with cold, influenza, viral pneumonia and other viral diseases.

However, it has been documented earlier that the patients diagnosed with colds and upper respiratory tract infections are given antibiotics in spite of the fact that 90% of these cases are caused by viruses (Willey *et al.*, 2007).

- Self medication: Drugs are consumed without consulting the qualified medical practitioners. This leads to the wrong choice as well as under dose of the drug. Thus, giving an opportunity to the microorganism to learn the drug resistance strategies; Self-medication with antibiotics may increase the risk of inappropriate use and the selection of resistant bacterial strains (Chalker, 2001; Grigoryan, 2007; Nalini, 2010).
- Incomplete medication course: the situation is made worst by patients not completing their course of medication. When antibiotic treatment is ended too early, drug resistant mutants may survive. The under or over prescribing may lead to drug resistance (Akkerman *et al.*, 2005).
- Use of antibiotics in feed supplements: Use of antibiotics as growth promoters in animal feed is another reason for emergence of resistant bacteria (Little *et al.*, 1986). The addition of low levels of antibiotics to livestock feeds do raise the feed efficiency and growth in cattle, pig, chicken (Pond *et al.*, 2005). There is an evidence of *Salmonella* Newport infection resulting from eating hamburger from beef cattle fed sub-therapeutic doses of chlortetracycline for growth promotion (Cromwell, 2001; Hay, 2005). The use of quinolone antibiotic enrofloxacin in swine herds appear to have promoted ciprofloxacin resistance in pathogenic strain of *Salmonella*.
- Antibiotics in daily toiletries: The spread of antibiotic resistance could be due to quite subtle factors eg. products such as soaps, deodorant, moth washes, cutting boards, baby toys often now contains triclosan and other germicides. There is an increasing evidence that widespread use of triclosan actually favours an antibiotic

resistance (Bamber and Neal, 1999).

Besides all the above mentioned points, skipping culture/sensitivity tests might be a factor leading to development of drug resistant strains. Antibiotics are administered without culture and sensitivity test. The broad spectrum drugs are given as substitute for culture sensitivity test with consequent risk of dangerous side effects, super infections and selection of drug resistant mutants.

Microbial preparedness, present scenario & future perspective:

Numerous reports have sprung up on emergence of drug resistant strains (Overturf *et al.*, 1974; Crossley *et al.*, 1979; Koornhof, 1980; Peacock *et al.*, 1981; Saravoltz *et al.*, 1982; Weinstein *et al.*, 1982; Hawkey, 1984; Archer *et al.*, 1985; Craven *et al.*, 1986; Cohen and Tauxe, 1986; Warren, 1986; Henderson *et al.*, 1988). The advent of newer drugs, the drug resistance pattern has also changed drastically with evolution of multi-drug resistant strains (Varaiya and Gogate, 1998). This change has posed a new challenge to the scientists across the world in respect of discovering new combat weapons for the microbial entities.

The miniatures have exhibited wonderful warfare strategies by developing new defense mechanisms. The ultimate goal seems to be nonetheless their survival and continuance of generation. A cold war between pathogenic microorganisms and the mankind is on. Scientists are busy with discovering effective antimicrobial molecules and on the same time the miniatures are excelling fast in evolving efficient virulence factors. Undoubtedly, scientists have done commendable job by discovering agents of control and elimination of these dreaded microorganisms. However, we could hardly boost of eradicating only a couple of the noxious microbial entities. Moreover, the expense per eradication or control in terms of resources, finance, manpower and time is beyond calculation.

Thus, there is a need to introspect and redraw the strategies for control and elimination of pathogenic organisms. Scientists have stressed the need for surveillance of isolates for antibiotic resistance (Adebayo *et al.*, 2012). Besides pumping our energies and resources in evolving new molecules, processes and technologies, the outcome of highly expensive researches need to be used judiciously to the benefit of mankind. "Prevention is better than cure" needs to be practiced in its true sense to nip the pathogen in the bud before it exhibits itself in uncontrolled proportions. The microorganisms are pretty smart and active in terms of multiplication, reproduction and emergence. *Neisseria gonorrhoeae* could learn to evade the effect of sulphonamides in just six years and took only sixteen years to resist the action of penicillin (Willey *et al.*, 2007). This implies that either the development of new antimicrobial molecules to be faster or existing molecules rendered effective for longer periods through our practices. Moreover, there is a need to view the drug resistance from social perspective and sincerely implement and practice the guidelines that are enforced as a result of proven research outcomes. Further, the ill effects arising due to non-implementation need to be undone. This would be a real payback to the hard earned innovations.

CONCLUSION

From social perspective point of view, curbing the menace of drug resistance could be viewed as a joint social responsibility. The government organizations, non-government organizations, clinicians, practitioners and each individual need to come forward to contribute for curbing the practices that lead to the emergence of drug resistant strains. It would not be absurd to state that the righteous approach towards the subject and sincere efforts along with major budget allocation for implementation of the research findings could shun the

burden of scientists and open up new and well executed front to fight the nuisance of drug resistance.

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