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Essential Amendments to Control Resistance to Antibiotics among Bacteria.

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ABSTRACT

Microbial resistance to antibiotics is gaining a lot of attention in the past few years. There has been a lot of debate in this regard but the outcome seems to be very disappointing. Added to the situation there are no proper data on per cent raise in antibiotic resistance. The growing threat from resistant bacteria calls for concerted action, to prevent the emergence of new resistant strains. Since the discovery and subsequent widespread use of antibiotics, a variety of bacterial species of human and animal origin have developed numerous mechanisms, which render bacteria resistant to nearly all known antibiotics. There are many virulent bacterial genera that are resistant to multiple classes of antibiotics. Infections caused by multidrug resistant bacteria have limiting treatment options, compromising effective therapy. In this regard the present article provides few parameters, which need to be implemented at various levels for efficient reduction of antibiotic resistance among bacteria.

INTRODUCTION

Resistance to antimicrobial agents a global menace is resulting in considerable morbidity and mortality from treatment failures. At the same time it necessitates the burden of increased health care costs [1]. Many of the greatest challenges in medicine and public health involve the evolution of drug resistance by pathogens. The Centers for Disease Control and Prevention (CDC) stated that in United States of America *Neisseria gonorrhoeae* is showing prominent drug resistance. CDC warns that gonorrhea can evolve as potentially untreatable forms of the disease. The susceptibility of gonococci's to antibiotics, such as cephalosporins, is diminishing and the situation is alarming [2]. In 2011 Japan announced that a new strain, H041, of gonorrhea has been discovered which is resistant to all forms of antibiotics. Worldwide, gonorrhea strains are resistant to at least one major class of antibiotics. Similarly, in United Kingdom the situation seems to be rampant. It is estimated that more than 25,000 people die every year in Europe from bacterial infections resistant to antibiotics. Therefore, the government of Canada recognizes the serious impact that antibiotic resistance has on individuals, their families and the health care system. The government is supporting two large research teams that will address this issue through collaboration between the Canadian Institutes of Health Research (CIHR) and the Medical Research Council (MRC) in the United Kingdom [3]. In India bacteria carrying a gene that confers resistance to a major class of antibiotics have shown up in samples of drinking water and sewage seepage from New Delhi. This raises the danger that people will be exposed to disease-causing bacteria that cannot be treated by antibiotics [4]. Moreover *Mycobacterium tuberculosis* may get resistance to all generations of antibiotics at any given time [5].

During the past few years tremendous progress has been made in the analysis of mechanisms involved among bacteria for drug resistance [6-8]. Most of the articles in scientific journals are concentrating mainly on the much known aspects of mechanism of resistance exhibited by microbes to antibiotics. The common resistance mechanisms reported till today are decreased drug permeability [9]; multidrug resistant (MDR) pump mechanism [10]; change of drug receptors [11]; changes in metabolic patterns to avoid dependence on a pathway that could be blocked using antibiotics [12]. Some articles are mainly oriented towards classifying the microbes to group of antibiotics for which they have

gained resistance [13].The articles are enriched with use and misuse of antibiotics by man that has resulted in antibiotic resistant among bacteria, but fail to provide solutions which can be universally applied.

Therefore, it is high time to have a practical input of action to curb the upper hand of microbes. In this regard the present situation demands some simple practical ways to really take down the situation to a satisfying level. The regulations should be more stringent not only for developing countries but also to the developed nations, where, antibiotics at higher dosage are being fed through cattle feed. The article is mainly oriented with facts prevailing at large in Asia including India, but the issue can be definitely discussed by any country in the world, as antibiotic resistance is a stark reality across the globe. Some of the easily amendable issues that need to be taken care are discussed below for amendment.

Role of Health Ministry/Governments

Issuing subsidy to antibiotic resistance test should be the priority that heath ministry should attend to. Government should intervene at least at the present context where there is some hope to fight back the situation. Presently, the test to detect resistance to antibiotic costs around Rs 200 to 300 per sample in most of the cities. The cost of diagnosis increases, but never can decrease in future. Most of the microbiologists do perform this test in laboratories for various research and teaching purposes. The cost price at which the test can be done is not more than Rs 40. This includes Stokes or Kirby-Bauer methods which include a medium (eg; Müeller-Hinton agar medium) and antibiotic impregnated discs, excluding non-technical charges.

At this level the Health Ministry should make it mandatory for the diagnostics labs to fix a price of Rs 40. The diagnostic labs should stop calculating their non technical aspects like staff and maintenance cost of laboratory. So that at least this test should be affordable to every man in the society. The Government of India has done a marvelous work, by introducing stringent laws against gender testing in the field of radiology, there by an excellent decline in female feticide has been achieved. Now, a similar type of strict regulation is required and the governments should enforce a law to the clinicians to compulsorily seek the aid of para clinicians, for every case requiring antibiotic prescription. Minimum Inhibitory Concentration test (MIC) should be performed to know the susceptibility of microbes to antibiotics and then the dose and type of antibiotic can be prescribed.

Role of Clinicians

The moral ethics is the key character of every civilized man. Clinicians should try to differentiate viral and bacterial infections to the maximum possible extent. But it is easier said than done, therefore wherever the situation demands clinicians should let go their reluctant attitude and commit themselves for the noble cause and demand a laboratory report of the infection causing pathogen and its susceptibility. The same should be mandatory for all including pediatric patients, but can exclude geriatric patients who may not be able to run around diagnostic labs and clinics.

Partitioning the consultancy chamber and using a part of it as a mini lab should be a better solution for the problem. Whenever a little space is available, an orthopedic will have his own radiology and physiotherapy chambers, a surgeon will have radiology lab in his premises (of course which includes their own medicine counters) why not a physician/ pathologists have an extra chamber at least wherever possible, which can accommodate just an incubator and a mini autoclave. The clinician himself can go for the MIC test with the assistance of a microbiologist and decide the type of antibiotic within 18 hrs. Thus the patient does not feel exhausted as he need not go in search of a pathology laboratory. Moreover this process is beneficial to the society at large, which should make its implementation a high priority issue.

Role of good Samaritans

Infected persons/ persons taking care should cooperate and do the essential visits for diagnosis, one visit to the clinician and one to diagnostic lab.

At this junction it is not the individual comfort that matters. It is for the welfare of the entire society that such trivial sacrifices need to be done and being a social animal one need to follow certain obligations.

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Role of Microbiologists

The faculty of microbiology can be of immense help in disseminating the knowledge by organizing special lectures on microbial resistance to antibiotics, in every city and village. A very important point to be taken care of by all microbiologists is the sensible use of antibiotics. During research and practical classes a careless attitude of application of antibiotics is being practiced all over the microbiology laboratories. In some experiments antibiotics are added as agents to control bacteria and promote the growth of fungi. It is a routine practice to deviate the dosage rules. In many cases when low dosage is applied to media the contaminant bacteria can easily gain resistance to antibiotics. Added to the problem, after the experiment the personnel involved never bother to autoclave the bacterial culture plates properly. If bacterial colonies survive improper sterilization, they may reach sewage creating a possibility of transferring drug resistance mechanism to coliform bacteria that may be present in the waste water.

The above situation demands a high level of responsibility from all those concerned. It is essential to go for alternate methods like lowering the pH of the medium or use of certain acids like tartaric acids which inhibit the growth of many bacteria allowing the growth of fungi. Use of dyes (eosin, malachite green, crystal violet) which selectively inhibit the common contaminant bacteria can also be applied according to the experimental requirement. Therefore in teaching and research laboratories the careless attitude should be curbed and the suggested methodologies can be incorporated.

The present article requires immediate attention from government and other public health agencies like world health organizations. In contrast most of the governments and heath care organizations are simply promoting research on synthesis of novel groups of antibiotics. Even though it is essential, it has many hindrances. To quote a few, it is a known fact that a novel drug design requires more than 15 years, the novel antibiotic should be made available as and when it is required. So concentrating only on drug designing and neglecting simpler ways to avoid resistance is not advisable. Moreover it is crucial to recognize that novel drug therapy is not a simple matter. A complex array of factors influences the effectiveness of drugs. Drugs need to be administered in several different ways and they do not always spread rapidly throughout the body or immediately kill all invading pathogens. The drug must actually be able to reach the site of infection and the pathogen must be susceptible to the drug. Therefore an effective antibiotic for the urgent need can only be procured from existing groups of antibiotics, by minor modification in their chemical composition. Which again becomes a temporary solution for the existing problem as the bacteria can easily express plasmid mediated antibiotic resistant genes to neutralize the drug. Hence it becomes essential to tackle the situations technically along with some of the non-technical issues, discussed in the present article. Meanwhile alternative therapeutic agents are being tried against bacterial infections but with little success. Among non conventional antibiotics bacteriophages provided some hope to control bacterial infections. The success rate with bacteriophages was too low. Further, considering the high mutation and evolution capacity of viruses it could be fatal to try out such procedures. Therefore lysozymes from bacteriophage are being tried as therapeutics for infections caused by bacteria. A lysozyme isolated from *Acinetobacter baumannii* phage has been tried against bacteria, and the research suggests that it is a good candidate for the control of nosocomial infections caused by multiple drug-resistant bacteria [14]. Even though results are encouraging it is short lived, as bacteria can easily gain resistance to lysozyme activity. Moreover application of these enzymes cannot be made target specific. Recently there are reports of silver nano particles being applied to treat bacterial infections [15, 16] that can be replaced by conventional antibiotics. Even though it is brim hope it can prove effective in comparison with bacteriophages.

Further, it is essential to note that the recent Amoxycillin plus Clauvanic acid combination and life saving Vanomycin are already being used indiscriminately. In the present scenario, where bacterial resistance is being reported continuously to traditional antibiotics, there is a great urgency to save these two antibiotics which can take care of almost all pathogenic bacteria known to medical science. It is threatening to know that even for such medications there are already reports of resistance by a few pathogenic bacteria [17]. Therefore implementation of few regulations discussed in the present article not only improves the present condition, but also provides the required time for developing a new generation of antibiotics. Presently Amoxycillin plus clauvanic acid combination can definitely provide some breathing space for the situation, provided it is used with sense, so that bacteria do not learn how to pump out this antibacterial combination from their cells. It is high time for the researchers to stop publishing the same old information with a few minor modifications on drug resistance which is already there and well documented.

CONCLUSION

The need of the hour is implementing certain regulations at various levels, as is described in the present article. Every technical person in the clinical and para-clinical field knows that we are forging towards a situation, where we go empty handed to fight bacterial infections. Already there are many speculations about uncontrollable infection

rates by an array of bacterial genera. Why wait for such situations? We can do better things than surrendering ourselves to bacterial infections. In view of this it becomes very essential for all the law makers, national and international scientific organizations to spare some time, think over and formulate regulations at each of the above discussed levels before the situation gets out of control. The facts discussed in the present article can definitely reduce the rate of antibiotic resistance among bacteria and can avoid unnecessary loss of human life.

indicates proposed implementation.

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