Evolution Of Multidrug Resistance Superbugs, A Healthcare Nightmare – Short Review

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Abstract: Antibiotics resistance are increasing. Public health officials are alarmed by the increasing frequency of antimicrobial- resistant microorganisms that have been remerged in the hospitals. There is sufficient tales to remind us that antibiotics might lose all the potency against invading bacteria. The development of resistance from the evolution of the elegant resistance mechanisms that create superbugs, which is spread by exchange resistance traits with other microorganisms. The Centre for Disease Control and Prevention estimates that more than 2 million people annually are sicken from the drug-resistance bacteria. The antibiotic resistance is particularly destructive in hospitals, where such infections strike the patients with chronic disease and weak immune systems. High risk groups includes individuals who have undergone recent surgery, the cancer patients, diabetics etc.Selection intensity is the major contributor to the resistance which can be determined by the volume of drugs consumption by human and agricultural industry. Cost to fitness of the microorganism is associated by acquired or De novo resistance. Therefore it is assume that reduction of the prevalence of resistance can be carried out by reducing the volume of drug use.
Keywords: Antimicrobial resistance; Multidrug- resistance; Conjugation inhibitors

Introduction

Microorganism have learned to adapt so that they can survive in the ever-changing environments. Numerous mechanism are adapted by superbugs that reduces or eliminates the cost of resistance, and such adaptation may minimize the potential benefits. There are countless examples of superbugs that represent an immediate threat to all patients and some which are threat to those patients that are immunocompromised. Growing antimicrobial resistance (AMR) is a serious global threat to human, animal and environmental health. This is due to the spread, emergence and persistence of multidrug-resistant (MDR) bacteria or ‘‘superbugs’’.

There is no signs of decline in the global antibiotic resistance, though it may perhaps shift direction. The multifaceted is the etiology of antibiotics resistance, and its consequences pose an impact across the world [1]. Number of attempt have been made to describe the diverse aspects antibiotic resistance. The success of modernized medicine are cancer therapy, a surplus of advanced major surgeries, organ transplantation might not have been possible without effective antibiotics treatment to control for bacterial infections. Effective global action plans has to be adapted soon to avoid the encounter of terrible complications for medical, social and economic prospects [2].

Mechanisms to facilitate the evolution and maintenance of superbugs

De novo resistance

Single or multiple genetic mutation results to the De novo changes. De novo genetics changes within the organisms leads to the development of resistance. Few examples of development of resistance are *Mycobacterium Tuberculosis* to streptomycin and *Staphylococcus aureus* to fluoroquinolones and development of spectrum β-lactamases in rifampin resistance [3,4]. Due to the random interaction and cellular operation all the organisms suffers to certain mutation. However the resistance offered by the selective pressure by the antibiotic exposure might have resulted from the adaptive mutation. Such mutation are called spontaneous mutation. Emergence of antibioitic-resistant strains by the selection of pre-existing mutants in population of bacteria exposed to antibiotics. It is the one of the important mechanism for the generation of resistance, especially to organisms under normal condition are not known to exchange DNA example Mycobacterium species [5, 6].

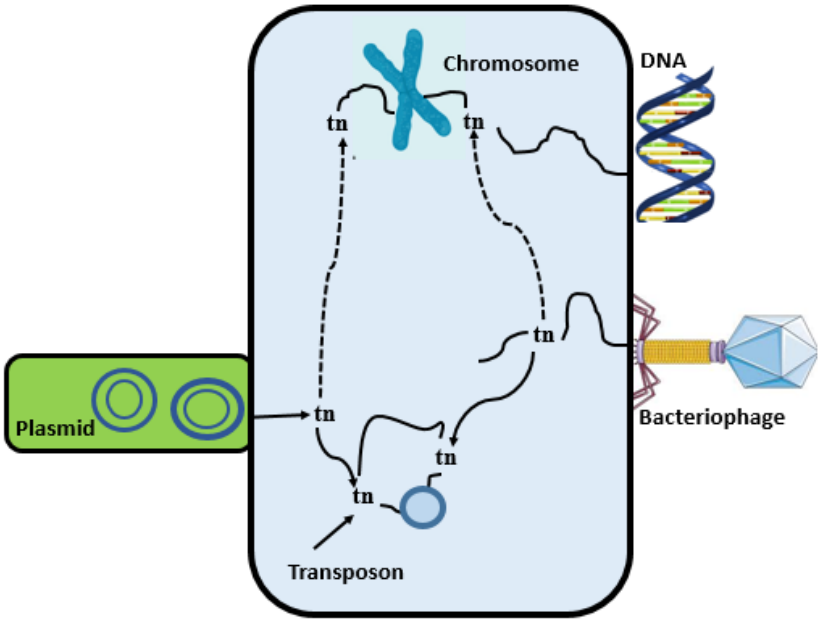

Fig. 1. Through variety of mechanism bacteria exchange resistance genes. Genes from one bacteria to another bacteria can deliver the extra chromosomal plasmids. A small DNA elements known as transposons (tn) can move various DNA elements: chromosomes, plasmids and bacteriophages. DNA can enter on plasmids between two cells through cellular uptake of naked DNA, through cell to cell contact (conjugation) between two cells, through bacteriophage introduction.

Acquisition resistance

In bacterial evolution horizontal gene flow is a driving force. Complex and elegant resistance mechanism are shared by bacterium, which may have evolve eons ago, with bacteria from other species within the same genus and with bacteria from other genera [7]. By three mechanism acquisition of foreign DNA occurs: transduction, transformation and conjugation. To closely related species transduction is limited by the high degree of specificity of the adsorption step in bacteriophage invasion. Similarly, transformation is confined to intrageneric transfer [8]. Neisseria meningitides and Streptococcus pneumonia take foreign DNA and incorporate it into their chromosomes. Mosaic penicillin-binding protein genes create accounted by this mechanism, which have reduced affinity for penicillin. Genes that mediate resistance are found on plasmids or transposons which by conjugation get disseminated among various bacteria (Fig 1).Despite belonging from different genera the gram positive and gram negative bacteria can transfer the resistance genes via the conjugative

plasmid. The conjugative transposons can extract themselves and incorporate into the recipient via conjugation emphasizing the point that they are self-transmissible elements. By site-specific integration, plasmids and transposons acquire multiple antibiotics-resistance determinants [9].

Strategies to combat antimicrobial resistance

Bacteria of different species shares MGEs that consists of common reservoir of DNA that is up to 20% of the bacterial panagenome [10]. It leads to the quick transmission of AMR genes among evolutionary divergent bacteria. The discovery of the new antibiotics are extremely important for the solution to fighting against infectious disease. Finding strategies and novel target to deal with the spread of AMR should probably be the best approach. The spread the AMR genes should mainly relay on the methods: i) alteration or combination of drugs, ii) approaches for discovery of drugs and iii) targeting bacterial fuctions which are essential for the infection[11].Some of the complementary approaches like prevention of existing therapeutics, decreasing the antibiotic consumption and general hygiene and containment. Discovery of conjugation inhibitors (COINs) is one of the interesting approach against the transmission of AMR. All bacterial infections cannot be cured by single antibiotics, bacteria having the resistance to one antibiotic may display a greater sensitivity to a second of distinct structural class. This phenomenon known as collateral sensitivity which has led to serious discussion to design a novel drug [12, 13]. Most feasible approach is the combination of different therapies. Alternative strategies may include: i) pro tempore use of available antibiotics (drug rotation or antibiotic cycling), this method subjected criticisms on the basis of lack of reliable clinical information, ii) implementation of biological approaches like new vacccines, phage therapy[14], use of antimicrobial peptides etc, iii)use of new small mlecules as antipersisters or antivirulence [15], iv) targeting bacterial-encoded virulence factors, v)serch of chemical derivatives of the known antibiotics. It therefore behoves us to look to other disciplines—such as population genetics, mathematical biology and ecology to help us tackle this unaccountable and important problem. Many other studies have been done in this regard with convincing findings [16-24].

Conclusion

We have witnessed the relentless dissemination and evolution of superbugs that possess resistance mechanism to them. This is due to the previous exposure of organism to antibiotics produced by other bacteria, by overuse and inappropriate use of antibiotics in human and agriculture. Knowledge regarding the extension of the AMR issues should be controlled by comprehensive, unfailing data collection. The scarcity of the novel antibiotics, the control of AMR seems difficult due to the inadequate information, one cannot predict future scenario with surety.to confront this issue multipronged strategies should be adopted. Refreshing and constant education of the physicians, pharmacists and medical students is required. As a part of policy strict monitoring of antibiotic should be implemented. All the elements of one health should be controlled as well as environmental and ecological aspects of the issue should not be ignored. It take years before to see the decline in the level of resistance even if we are able to ensure the appropriate use of antibiotics because many bacteria have been able to reduce the costs associated with resistance. This means that we must develop better ways of preventing and treating infection due to these superbugs.

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