



Review Article

A GLIMPSE OF INFECTION AND RESISTANCE: A REVIEW

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ABSTRACT

Antibiotic resistance is a global phenomenon with ancient origins antibiotic resistance which is regarded as a priority threat by WHO. In fact antibiotic resistance is an inevitable consequence of antibiotic use irrational use enhances the rate of antibiotic resistance the irrational use has made conventional methods for combating antibiotic resistance nonresponsive and had led to emergence of multiple drug resistant infections. This led to exploration of novel ways to fight antibiotic resistance. In spite of all these efforts antibiotic resistance is still a global threat and could be managed by rational use of drugs and methods whether conventional or novel methods. This review gives a glimpse of antibiotic resistance and the conventional and novel methods to fight it.

Keywords: antibiotic resistance, resistance, infection

INTRODUCTION

Infectious diseases were prevalent in prehistoric times which could be traced through evidences of small pox found in 3000 year Egyptian mummy and poliomyelitis in Ereb papyrus paintings.¹ In the past primitive tribes attributed the causes of diseases to linked diseases to magic/ nature and prayers were first attempts to treat them². In Asian countries, herbal and traditional medicines are continuously being used against several ailments³. In India, Ayurveda a natural system of treatment has been practiced for more than 5,000 years.⁴ Likewise traditional Chinese medicine originated in China at least 3,000 years ago and spread to overall throughout the east Asia. Besides these traditional Unani medicine, traditional Korean medicine and traditional, Native American medicine have also originated world wide long back ago. Synergy in all forms of traditional medicine is the use of medicinal plants in the treatment of disease and the maintaining health.⁵ In pre antibiotic era infections as meningitis and endocarditis were fatal.⁶ In golden age of antibiotic infection decreased but resistance emergence due to irrational use of antibiotics. Infectious diseases are presently the world's largest killer of people with India having its highest burden due to pneumonia, tuberculosis, diarrhoea, malaria, and measles causing higher usage of antibiotics⁷ leading its irrational use and emergence of bacterial resistance presently a global problem also regarded as one of the 3 major problems for human health by WHO.⁸ Factors of resistance are pathogen specific (virulence, transmissibility, survival fitness, previous trend), Prescriber specific (prescribing skill, knowledge path physiology pharmacokinetics, training) Patient Related (Self-medication, knowledge, adherence, OTC use)⁹ Mechanism of resistance is of 2 forms biochemical including mutations, hydrolysing enzymes, efflux pumps and genetic covering conjugation, transformation, transduction.¹⁰ Finally prevention of resistance can be done by prudent/ rational use of antibiotics⁴, imparting awareness¹¹, providing education¹¹, initiating hospital infection control programme¹¹/hand washing⁸, antibiotic rotation like mixing and

cycling¹², maintaining house hygiene¹¹, promoting new antibiotics development⁸, using combination therapy¹³, vaccination¹³, probiotics¹³, trace elements (selenium, zinc)¹³, phytochemicals¹³, union therapy¹⁴, apitherapy¹⁵, photodynamic therapy¹². Recent/Novel approaches includes use of viruses that can infect bacteria and also have antibacterial activity commonly known as phages. These are administered through oral, rectal, or iv routes and acts in 2 ways one lytic and other lysogenic major side effects of phage therapy include endotoxin release. Second novel approach is use of bacteriocins which are the bactericidal peptides having antibacterial properties. They interact with the cell membrane leading to change in its properties causing cell death. Secondly It may also bind to lipid-II facilitating transport of peptidoglycan subunit from cytoplasm to cell wall thus blocking cell wall synthesis causing cell death. Alternatively they can cause cell death by membrane de-energizing (IMF) or can also cause inhibition of amino acids uptake, exclusion potassium ions, cyto membrane depolarisation, cellular ATP hydrolysis and partial efflux. Advantages of bacteriocin therapy are easy degradation to nontoxic metabolites. Third strategy is using killing factors released by bacterial cells to kill sibling cells during starvation as an antibacterial. Chemically they are peptides and have been tested successfully against methicillin-resistant *S. aureus* and *S. epidermidis*. Fourth approach is using non antibiotics which are drugs used for non-infectious diseases but having microbial activities eg barbiturates, beta-adrenergic receptor antagonists, diuretic, antihistamines, mucolytic agents, non-steroid anti-inflammatory drugs, proton pump inhibitors and psychotherapeutic agents. These act by altering cell permeability, affect microbial efflux pump, cross membrane ion transport, cell energy transfer, membrane bound enzymes. Fifth approach is combining antibiotics with non-antibiotics eg penicillin and benzothiazine for MSRA advantage being the safety profile of non antibiotics is established side effect being dose for antibiotic use as compared to conventional use. Sixth approach is to target quorum sensing the microbial cell communication plays role in onset of virulence. Two mechanism are present one involving

signal detection through cytosolic transcription factor while other mediated by auto inducing signal detected through membrane receptor. Impairing this system can help to combat virulence of the microorganisms without imposing selection pressure. It enhances activity of antibiotics and restricts evolution of drug resistant strain.¹⁶ Other strategy is aiming the CRISPR-Cas system, which is a part of the immune system in many bacteria for protecting bacteria from viruses. Another approach is using of silver which has property to weaken bacteria and making them more susceptible to antibiotics. In addition using silver in combination with existing antibiotics can increase their effectiveness. Next approach is developing a candidate drug that disarms bacteria instead of destroying. Researchers based at VIB are exploring ways to inhibit the pilus formation mechanism.¹⁷ Presently recent explored novel approaches include modification of old antibiotics as B lactams, flouroquinolones, exploring microbial genome sequencing wherein bacterial genomes have given new targets for antimicrobials. Bioinformatics techniques based on open reading frames for identification of new targets especially for respiratory antibiotics. Combinational chemistry has wide role in antibiotic discovery requires screening of natural and synthetic compounds, exploring new targets like peptide deformylase, non malvonate pathway, bacterial fatty acid synthesis¹⁸, targeting non multiplying bacteria¹⁹, advanced nano biomaterials²⁰, FimhInhibitors²¹, bacteriophages²², antimicrobial peptides²³, Synthetic biology methods like recombinant engineering²⁴, and bacterial cell-cell signaling²², I Chip methodology for novel antibiotics production²⁴, biosensor applications²⁵, stimuli-responsive nano antibiotics²⁶, anti-virulence therapy^{22,27,28}, reducing in the bacterial load by hemofilters²⁹, host-directed therapy³⁰, anti-adhesion²⁷, quorum quenching²², bacterial small RNAs (sRNAs)³¹, marine drugs like Pseudovibriospesies.³², modulating human microbiota³³, using cow urine³⁴, Antibiotic Lysocin E screening by a silkworm model of bacterial infection.³⁵and union therapy¹⁴. Finally antibiotic resistance is an inevitable consequence of antibiotic use and follows darwinism laws of evolution.³⁶ hence could be combated only by proper, rational and judicious use of antibiotics, novel methods, conventional methods or else it would become an uncontrolled threat globally.

CONCLUSION

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