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ANTIMICROBIAL RESISTANCE (AMR) IN KAUMARBHRITYA: AN AYURVEDIC VIEW

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ABSTRACT

Antimicrobial resistance (AMR) is a global concern. New resistance mechanisms are emerging and spreading globally. When micro-organisms become resistant to most antimicrobials, they often referred as "superbugs". We are surrounded by billions of microorganisms. Most of them are not harmful, or are opportunistic which may attack in hosts and children. They may prove harmful in neonatal wards or labour room. Limited ability to manage resistant infections results in prolong morbidity, disability and increased mortality. AMR is natural phenomenon. However, it is accelerated by the inappropriate use of antimicrobials. It is quite natural that Ayurveda, the oldest health care system in the world (about 5000 years old) does not have the word 'Antibiotics', but a curious search in its literature will definitely shows number of references stating that certain disease are produced due to micro-organisms (krimi) and acharya have already mentioned many drugs and kalpa to kill these micro-organisms/krimi. The paper summarizes the Ayurvedic approaches which can be used effectively for prevention and treatment of bacterial diseases.

KEYWORDS: Antimicrobial resistance, AMR, Ayurveda, Krimi, Alternative Medicine.

INTRODUCTION

The word antibiotics is derived from two Greek words "Anti" means "against" and "Biotics" means life; here life form is represented by bacteria. The existence of unseen microbes was suspected from ancient times.[1] These single celled creatures have threatened humanity with infection which had high mortality and morbidity.[2] These microorganisms have potential to

spread infection at a very rapid rate and to cause widespread epidemics.[3] Antimicrobial resistance (AMR) is one of the world's most serious public health problems.[4] Many of the microbes that cause infectious disease no longer respond to common antimicrobial drugs (antibiotics, antiviral, antiprotozoal drugs).[5] Effective antimicrobials are no longer available which could cure virtually all bacterial infections. A high level of drug resistance is reported in *Enterococcus aecium, S.aureus, Klebsiella pnuemoniae, Acinetobacter baurmannii, P.aeruginosa* and the Enterobacter spp.- together referred by the acronym ESKAPE which cause the majority of the infections with in the hospital environment.[6] The wide range of AMR mechanisms used by the ESKAPE pathogens, includes enzymatic inactivation, modification of drug targets, changing cell permeability through porin loss or increase in expression of efflux pumps and mechanical protection provided by biofilm formation. It is estimated if there is a continued rise in resistance levels, by 2050 it would lead to 10 million deaths annually.[7,8] Additionally, AMR leads to longer hospital stays, higher rate of hospitalization and rise in the treatment cost.[9]

Bacteria are commonly defined as MDR, extensively drug resistant (XDR), pan drug resistant (PDR). The term MDR applies to resistance to at least 1 agent in more than or equal to antimicrobial classes, XDR when there is resistance to all except 1 agent in less than or equal to 2 antimicrobial classes and PDR when the isolate is resistant to all available antimicrobials.[10] AMR is an age-old phenomenon. Most antimicrobial compounds are naturally produced and coresident bacteria in the environment have evolved mechanisms to overcome their action in order to survive.[11]

The key mechanisms responsible to antibiotics in bacteria are listed below.

- **Plasmids:** Both chromosomal mutations and / or genetic transfer are responsible for acquisition of resistance, it is the transferable resistance which poses a greater threat as it can achieve much wider dimensions due to rapid dissemination. R plasmids play a vital role in carrying this transferable resistance. A single plasmid can harbor several genes coding for multiple drug resistance.[12]
- **Inactivation of antibiotics:** Bacteria may produce enzymes that chemically modify or degrade antibiotics and inactivate the drugs.[13] For example, penicillin resistance in *S. aureus* is because of the production of enzyme ß-lactamase that inactivates the antibiotic by hydrolyzing the ß –lactam ring.[13]

- Target site modification: The molecules that are normally bound by an antibiotic are normally altered or replaced and thus essentially eliminate the drug's target in bacterial cells. An example of this mechanism is Methicillin resistance is Staphylococci due to the presence of mec A gene which encodes for PBP 2A.[14]
- Prevent drug uptake: The entry ports for the drugs can be eliminated by bacteria by altering permeability.[15] It has been reported that *P. aeruginosa* can develop resistance to imipenem by mutational loss of porin proteins thereby modifying the outer membrane permeability.[16]
- **Efflux pumps (EP):** there are 5 super families of microbial efflux systems viz. NorM, multi-antimicrobial extrusion protein family (MATE), QacC small multidrug resistance family (SMR), resistance nodulation cell division (RND).[17] These EPs are responsible for the export of antibiotics before they find their intracellular targets.
- **Biofilm formation:** Biofilm is formed by a complex aggregation of microbes, wherein the cells are embedded matrix of extra cellular polymeric substance (EPs) (self-produced). Production of biofilms through adherence of bacteria to human tissues and medical devices is a major virulence factor associated with increased antibiotic resistance, reduced phagocytosis, and overall persistence of the microorganisms.[18]

Adaptation to the antibiotic environment seems to occur very quickly in an evolutionary timeframe. India has emerged as the world's largest consumer of antibiotics with 62% in popping habits in last decade. Irrational use of antibiotics may increase the resistance in individuals, on the community level and in the society as a whole. Increased trends of self-medication and poor adherence of dosage may also lead to antimicrobial resistance.

Concept of microbiology in classics

It is quite natural that Ayurveda, the oldest health care system in the world (about 5000 years old), does not have the word 'Antibiotics', but a curious search in its literature will definitely shows number of references stating that certain disease are produced due to micro-organism (krimi) and Acharya have already mentioned many drugs and kalpa to kill these micro-organisms/ krimi.

In Rigveda, micro-organisms are described as invisible organism having specific unique characteristic. And in Atharvaveda it is mentioned as sukshma jantu. Charak Samhita classifies organisms into normal (sahaja) and the pathogenic or the invaders (agantu). The

pathogenic parasites are further classified into those that grow on the external surface or internal environment of the body termed as krimi. In various ayurvedic classics, Acharyas have beautifully explained the term Graha which capture human and produce variety of symptoms.

Another interesting thing can be noted in these references which is, Ayurveda has not only advised on destroying these disease producing organisms but has also stressed that one should also increase the resistance power (immunity) against these organisms to prevent the relapses of the disease. Usually sweetish substances, oily substances and kapha Vridhikara Aharas with alkaline pH inside the gut produces a favorable environment for the growth of the worms.

Hence, those methods, drugs, food materials which destroys this favorable environment like Katu, Ushna, Kashaya, Tikta rasa should be administered as a treatment procedure.

Prevention of antimicrobial resistance

Prevention is the measure taken by an individual prior to the onset of any disease, which will remove the possibility of the disease occurring in the future. Ayurvedic principles related to prevention is widely accepted globally due to its safety and cost effectiveness. The following points mention can be considered for the concept of health education.

i. Dincharya – Daily regimen to be followed by an individual.
ii. Ritucharya – Seasonal regimen to be followed by an individual.
iii. Samshodhana – Seasonal cleansing of the individual.
iv. Adhaaraniya Vegas- Non-retention of the natural urges.
v. Rasayanas – intake of Rasayanas.
vi. Sattvavijaya – improving the mental strength with the help of Yoga and Dhyana.

For strengthening the host, promote health education related to daily regimen, night regimen, seasonal regimens and Achar rasayan.[19]

Curative care through Ayurveda

Aparkarshana, prakrtivighata and nidana-parivarjana are the basic treatment measures mentioned in Ayurveda classics against microbes. Therapeutically it can be correlated with the term sodhana , saman and nidan parivarjana respectively.[20]

Panchakarma like sirovirecana, vamana, virecana, asthapana are pointed for apkarsana therapy.[21]

Antagonist drug therapy for destruction of infectious agent and reduction of symptoms is achieved through prakritivighata and is performed through the drugs used in krimighna and jvarahara like Mahakashayas.[22]

Mahakashyas mentioned in our Ayurvedic classics are having Visaghna, Vranasodhana, Vranaropana and kleda-puyopasosana activities. The ultimate aim of all these drugs is to arrest and encounter the infection. Main action of these drugs is to encounter the visha or antigen caused by the microbes. Krimighna, kandughna, kushthaghna, jvarahara, Svasahara, Kasahar, Sothahara, Sitaprasamana Mahakashayas are to be used against these symptoms.[23] Some groups of drugs in mahakashaya are also used to arrest the infections caused by specific type of microbes which produce different types of discharges, burning sensations, pain, redness etc.

Aarvadhadi mahakashaya having kushtagna and kandugna activity destroy the microbes, alleviates itching and cleanses wound; Salasaradi group is also having kushtagna activity and administered in various types of infective skin diseases; Varunadi group is having Vranaghna activity and is highly effective in internal abscess; Lodhradi are yonidoshahara group which arrests the disease of female genital tract caused pathogens; arkadi group cleanses infective wound; Surasadi group is highly effective in respiratory infection both upper and lower tract.

Anti-Bacterial Herbs

There are many herbs and its kalpas which are having anti-bacterial properties and are being used today. These herbs are not only effective but also proved to be safer more than modern antibiotics. These are Haridra (turmeric), Tulsi (Ocimum sanctum), Guggul (Commiphora mukul), Neem (Azadirecta indica).

Pippaladi group is effective in acute and chronic rhinitis; Eladi group is highly effective in boils and furuncles; Vacadi and Haridradi both encounter the pathogens in the diseases like diarrhoeal disorders; Trinapanchamul is highly effective in urinary tract infections.

Amra: The leaf extracts revealed antibacterial action against B. subtalis, Staphylococcus and vibrio cholera. It has antifungal properties against candida.[24]

Kutaj: The Therapeutic effect of this plant in amoebiasis is well known. Its active ingredient is conisedered. Fruit extract showed (50% ethanolic) antiprozoal effect against Ent histolytica. Clinical studies have been done which show excellent effect in amoebiasis and giardiasis.[25]

Gokshur: It has nephroprotective effect against Gentamicin induced nephrotoxicity. It acts reducing free Radicle release (MDA) at the nephrons.[26]

Bhumyamalaki: indicates a small plant simulating Amalaki. This plant is described in ayurvedic classics, Brhattrayi (charak samhita, susruta samhita and Ashtanga Hridaya) by the names of Tamalaki and Bhudhtar and is used in Swasa, kasa.

A clinical trial had been done where Bhumyamalaki has been taken as Phyllathus niruri linnamarus for the treatment of viral hepatitis B.

Chemical constituents :- two main chemical constituents have been isolated Phyllanitin and Hypothyllantin . Anti HBs like activity of Phyllanthus niruri has also been described in both vitro and vivo models using whole plant extract. There are also indications that Phyllanthus niruri extract may be helpful in interrupting the hepatitis B virus carrier state.

Extract of Phyllanthus niruri inhibits the reaction between HBsAg and the antibody to it (Anti- HBs) Hep B virus contains an endogenous DNA polymerase which is required for its replication. It inhibits the endogenous DNA polymerase of Hep B virus. It is postulated that this drug may have an action with antibody binding sites on HBsAg, which prevent further proliferation of Hepatitis B virus. Bhumyalaki Rasayan vati and its clinical trial on the patients of viral hepatitis B revealed encouraging results. Bhumyamalaki is a dependable drug for treatment of viral Hep B as well as carrier state of Hep B.[27]

The importance of Ayurveda in global scenario is because of its holistic approach towards positive life style. It deals with both the preventive and curative aspects of diseases. Ayurveda mentions the treatment modalities as topical (bahi-parimarjana), systemic (anta-parimarjana) or by surgical intervention. Fumigation (dhoopana) catergorized under topical (bahiparimarjan) treatment, has been told as a treatment in all the classics of Ayurveda but detail description is available only in Kashyap Samhita in a chapter named ‘Dhoopakalpa’. Fumigation (medicated smoke) creates an aseptic environment, kills microbes and thus,

prevents infection. Ayurveda have provided an elaborated explanation of many herbal drugs which may prove to be safe, effective and lucrative in present settings.

Nimba (Azadirecta indica): its active constituents possess insecticidal and insect repellent activity, like 22, 23-dihyronimocinol extracted from leaves and azadirachtin extracted from seeds. A.indica fumes against streptococcus payogens after 10 mins exposure showed 100% inhibition and 50% inhibition after 5 minutes exposure, it also showed inhibition of s.aureus, s epidermis, and p.aeruginosa under same settings. Azadirachta indica is effective against head lice in topical use.[28]

Guggul (Commiphora wightii)

Extracts of guggul were evaluated for their potential antimicrobial activity against both gram positive and gram negative bacterial species of clinical significance. Ethanol extract was found to have comparatively higher activity than other organic and aqueous extracts of guggul. Gram positive bacteria showed competent but various susceptibilities to all the tested extracts. Some of the extracts exhibited significant inhibitions of bacteria even at low concentrations.[29]

Sarshap (brassica compestris)

Brassica species contain contrasting profiles of glucosinolates which have biocidal activity on different pathogens including bacterial and fungi. Fumigation with brassica species is effective against nematodes.[30]

Concept of Kumaragara

This emphasizes maintenance of healthy environment for children. The bed, clothing, blankets, furniture etc of child should be cleaned and fumigated wit rakshoghna dravyas like sarshap, guggul etc. the neonate after nama karan on 11th day should be transferred from Sutikagara to Kumaragar. This is done for the purpose of special nursing care so as to prevent drastic infections.

CONCLUSION

To conclude, Ayurvedic interventions can be used effectively for prevention and treatment of bacterial diseases. Ayurveda herbs have great potential as anti-microbial against local as well as systemic pathogens and they can be used in the treatment of infectious diseases. The literature used justifies the use of these herbal preparations in medical practice. However, the

range of efficacy is not established and hence such comparative studies are needed to be done. Hence in current era of AMR Ayurvedic interventions will go s long way in reducing the risk of development of AMR and also in alleviating the adverse effects of antimicrobial therapy.

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