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Relevance of Bacterial Normal Flora in Antimicrobial Resistance And Incidence of Pathogenic Infections and How to Overcome this Resistance

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Mini Review

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ABSTRACT

Antibiotic resistance represents a pressing problem, normal flora is destroyed by unnecessary use of antibiotics and as a result, microorganisms with resistance genes multiply. One side effect of misusing antibiotics is the transfer of resistance genes between Normal flora and bacterial pathogens, so we need to rationalize our use of antibiotics or find an alternative to them.

INTRODUCTION

There are some factors that contribute to bacterial resistance such as unnecessary use of antibiotics, using a very low dose of antibiotics and consequently, antibiotic doesn't kill microorganisms allowing them to multiply and spread infection, also resistance can be developed by a too-short duration of antibiotics or incorrect dosage of antibiotic [1,2]. Moreover, antibiotic resistance is natural as resistance genes can code protein which could degrade the B-lactams, tetracyclines, and glycopeptide antibiotics [3].

NORMAL VAGINAL FLORA AND BACTERIAL VAGINOSIS

Lactobacilli play an important role in maintaining the female genital tract by some mechanisms, such as producing lactic acid that decreases vaginal PH and prevents the occurrence of pathogenic bacteria, hydrogen peroxide, bacteriocin, and surface binding protein which in turn can reduce the risk of bacterial vaginosis. When lactobacilli decrease, there is a reduction of hydrogen peroxide and consequently, overgrowth of facultative anaerobes occurs and bacterial vaginosis happens as facultative anaerobes can displace lactobacilli then rise in vaginal PH(4_7). Furthermore, changes in innate immunity are responsible for the conversion of normal vaginal flora such as lactobacilli to facultative anaerobes that cause bacterial vaginosis [4-9]. Ethnicity is a crucial think about vaginal colonization by various bacteria and women of African ethnicity are more exposed to bacterial vaginosis than Caucasians [9,10].

NORMAL OCULAR FLORA AND ITS RESISTANCE

Under normal conditions, normal bacterial flora, tears, and eyelids help in protecting the eye surface from foreign microorganisms, consequently, no overgrowth of microorganisms can occur [2]. Some factors can make changes in the ocular surface flora such as geographical distribution and climate as in warm, humid weather, positive bacterial rate increases [11,12]. Another factor that contributes to influence ocular flora is alcoholism and it had been found that with chronic alcoholism, there's a higher incidence of *Staphylococcus aureus* compared to healthy ones [13]. Diabetes also has an effect on ocular flora, an investigation into the ocular flora of diabetic patients, the study found higher rates of methicillin resistance [14]. Antibiotic resistance can be developed by mutations and genetic exchange. The presence of genes of intracellular adhesion can form a biofilm in *Staphylococcus aureus* and Staphylococcus epidermidis and as a result, causing infection [15].

ORAL MICROBIAL FLORA AND DISEASES

The oral microbial flora can maintain the balance in the oral cavity. However, any change in the microbial ecosystem can lead to the growth and proliferation of pathogenic microorganisms like *Streptococcus mutans* and induce oral diseases like dental car-

ries due to alteration in the microflora. In addition, candidiasis is caused by a fungus, *Candida albicans* which is a component of norma oral flora but any change in the oral flora or during immune suppression can result in candidiasis which is an opportunistic fungal infection [16].

ROLE OF INTESTINAL MICROFLORA IN IRRITABLE BOWEL SYNDROME

Irritable bowel syndrome is characterized by abdominal bloating, variable bowel habits, and abdominal pain. Disruption of intestinal microflora can lead to irritable bowel syndrome due to the malfermentation of food because of decreasing numbers of Lactobacilli and bifidobacteria and increasing numbers of facultative organisms such as *Streptococcus spp, Escherichia coli and Proteus spp* [17].

NEW APPROACHES TO COMBAT BACTERIAL RESISTANCE

Bacteriophage therapy

Temperate phages can work as gene-delivery vehicles by transferring genetic material to bacteria through integrating their DNA into the bacterial genome, consequently, sensitization of nosocomial pathogens and bacterial flora on the skin of hospital personnel. Furthermore, the resistant pathogens now contain genes carrying sensitivity to antibiotics so resensitization of resistant pathogens occurs. On the other hand, we can use phage products like lysins which work as enzymes to hydrolyze bacterial cell walls, in addition, the T7 phage gene product 0.4 is able to directly prevent FtsZ, an important bacterial protein in the division process [18-20].

Photodynamic therapy

Photodynamic therapy uses visible light, harmless photosensitizers, and oxygen present in cells to overcome infections, then excitation of photosensitizer molecules occurs and causes the production of reactive oxygen species, consequently, bacterial cell destruction and death happen. On the other hand, multidrug-resistant pathogens can be damaged by using near-infrared light that potentiates the effect of erythromycin, ciprofloxacin, and tetracyclines which are multidrug efflux systems substrates and as a result, efflux inhibition may be due to near-infrared light [21,22]. Furthermore, photodynamic therapy can be used against biofilms, for example, Helicobacter pylori, a bacterium that forms biofilms and accumulates porphyrins that act as endogenous photosensitizers. By application of 405 nm endoscopic light, the reduction of CFU counts by 90% happens [23].

Role of vaccines in overcoming the antimicrobial resistance

Vaccines can be used for protection and reduction of colonization by inducing helper T cell responses as in pertussis vaccine that induces th1 and th17 responses [24,25]. Furthermore, directing vaccines against resistant pathogens or against factors of resistance is another approach to control antimicrobial resistance [26,27]. Also, we can use vaccines against virulence factors such as toxins and adhesions [24].

The antimicrobial activity of plant extracts

We can use plant extracts with antibiotics in order to inhibit the efflux pump, resulting in the accumulation of the antibiotic in the bacterial cells [28]. This strategy represents a synergy between antibiotics and plant extracts as plants have some advantages like fewer side effects, inexpensive and can be used as antimicrobial like alkaloids, flavonoids, and tannins [29].

Cationic antimicrobial peptides

They are broad-spectrum bactericidal against resistant pathogens, driven from natural sources like bacteria, fungi, insects, fish, and mammals as a response to infection. They can be used to kill Gram-positive bacteria and Gram-negative bacteria, evolved viruses, and even cancer cells *in vitro*. Furthermore, cationic peptides can induce the uptake of antibiotics and thus show synergy with antibiotics [30]. Also, peptide antibiotics can be used against malaria, trypanosomiasis, and filariasis [31].

CONCLUSION

In order to inhibit bacterial resistance, we need to prevent the transfer of resistance genes between normal flora and bacterial pathogens. Also, we must maintain our normal flora to help us overcoming bacterial resistance by decreasing misusing or overusing antibiotics and choosing the right antibiotic with a specific dose and finishing the course of treatment even if the symptoms are improved. Furthermore, we need to find an alternative to antibiotics and apply new approaches like bacteriophage, natural peptides, photodynamic therapy, and vaccines.

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