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BACTEREMIA ASSOCIATED WITH PROBIOTIC USE IN MEDICINE AND DENTISTRY

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Abstract: The effect of probiotics in systemic health is well documented. There are several advantages using of probiotics , but in some persons it carries the risk of causing bacteremia and sepsis. Probiotic treatment is adviced for the prevention and treatment of a number of diseases, and there is strong evidence for their efficacy. Probiotics are now widely used in many countries . Because of the increasingly widespread use of probiotics, a thorough understanding of their adverse effects and benefits is necessary. In this study the safety of probiotics and risks of probiotic use is discussed. Although probiotics have a good overall safety record, they should however be used with caution in certain patient groups such as premature infants , patients with immune deficiency and patients who undergo dental manipulations or dental surgical procedures.

Keywords: Bacteremia, Probiotic use , Medicine , Dentistry , Lactobacillus

I. INTRODUCTION

Probiotics are bacterial cultures or live microorganisms given as supplement that exhibit beneficial effects for the intestinal and oral microbial balance of the host. The term probiotics was introduced by Lilley and Stillwell in 1965. The beneficial bacteria were so named because they are pro life to humans.

USE OF PROBIOTICS IN MEDICINE

Probiotics have been used for prevention of intestinal infections, treatment of antibiotic associated diarrhea and intestinal malfunction and prevention of Clostridium difficle diarrheae. Use of probiotics in suppression of Helicobacter pylori infections and prevention of allergic diseases has been proved. Probiotics is also being used for favouring Calcium absorbtion in lactose intolerance patients. Use of probiotics in prevention of colon cancer and progression of HIV is under research[15].

Species used[16]: Probiotics can be bacteria, yeast or moulds but bacterial species are predominantly used. Bacteria commonly used are:

- LACTOBACILLUS
- BIFIDOBACTERIUM
- LACTOBACILLUS BULGARICUS
- STREPTOCOCCUS THERMOPHILU
- SACCHAROMYCES BOULARDII

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USE OF PROBIOTICS IN DENTISTRY

The use of health promoting bacteria for therapeutic purposes is one of the novel and latest approaches in dentistry. Probiotics are useful in promoting oral health and in prevention of dental caries and periodontal diseases.

Probiotic bacteria is recently being used in dentistry as **oral replacement therapy** where probiotics adhere to dental tissues as part of the biofilm or plaque and compete with the cariogenic and periodontal pathogens for colonization and hence prevent caries, gingivitis and improve oral health[16]. A great advantage is the ease of administration in the oral cavity. Live cultures can be used in a patient's mouth as there is no danger from stomach acidity as in the GIT. Probiotics lower the ph in the oral cavity so that plaque forming bacteria cannot form plaque and calculus. One of the most important benefits of probiotics in the oral cavity is reduction of inflammation. Probiotics can help fight harmful bacteria in the oral cavity and helps in maintainenece of healthy teeth and gums. Since probiotics is an all natural treatment it should not have any side effects.

LACTOBACILLUS

Lactobacillus is a gram-positive, microaerophilic or facultative anaerobic, rod-shaped bacterium that is part of the normal flora of the oral cavity, gastrointestinal flora, and genitourinary tract. Probiotic strains of Lactobacillus species are utilized in a variety of clinical practices with limited evidence to support their use. A large mumber of medical practitioners have proposed benefits of probiotics in treating diarrheal diseases, irritable bowel syndrome, children with atopy, prevention of urogenital tract infections, and prevention of pouchitis. However, the mechanism of benefit of probiotics is not completely understood[5]. It has been proposed that probiotics in the gastrointestinal tract may enhance intestinal barrier functions, stimulate immunity, and modulate inflammatory diseases. It has also been suggested that probiotics can inhibit infection and restore gut homeostasis by having a direct bactericidal effect on pathogenic bacteria and by inhibiting pathogen and toxin adhesion to the intestinal epithelium. Despite limited evidence, many patients use probiotics, believing in their efficacy without consulting their physicians. Serious infections with probiotic strains of Lactobacillus are not common. The bacterial strains are usually difficult to culture and identify and are typically considered contaminants[6]. A few cases, however, have been reported mainly in immunocompromised hosts where the bacterial strain isolated from the specimen was indistinguishable from the probiotic strain taken by the patient. Probiotic strains of Lactobacillus are currently used in a variety of clinical practices with limited evidence to support their use[19]. Lactobacillus species however can cause bacteremia and sepsis if they enter the blood stream.

II PROBIOTIC DELIVERY

Probiotic bacteria are normal commensals of the intestines. The probiotic bacteria for research are not only isolated from fermented food but also from healthy humans[8]. Probioitics can be provided in food by : Beverages ,Prebiotic fibres , lyophilized dried and packed into tablets, straws, chewing gums , dietary supplements , milk and milk products.Formulation: A formulation of approximately 10^8 probiotic bacteria per gram or milliliter (10^8/ml) with a daily intake of 1.5 – 2 dL per day is the recommended dose. For dental uses probiotics can be given in the form of lozenges, sucking tablets and chewing gums in replacement therapy[16]. Recent research approaches in dentistry have also used probiotics in toothpastes and mouthwashes.

III RISKS ASSOCIATED WITH PROBIOTIC TREATMENT

Probiotics are usually safe and well tolerated, when taken orally. There are common adverse effects like bloating, flatulence and constipation, but these effects are mild and go down with when used continually. One great concern in the use of probiotics is whether the viable organisms used in probiotics can move from the gastointestinal tract or oral cavity

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to cause systemic infections? Another major theoretical concern in the use of probiotics is whether there can be possible transfer of antibiotic resistance from probiotic strains to pathogenic bacteria[19].
Probiotics are mostly given as dietary supplements rather than as pharmaceuticals or biological products. Therefore it is usually not necessary to demonstrate the safety, purity, action and potency of a probiotic, before marketing probiotics. This can lead to inconsistencies between the stated and actual contents of probiotic preparations. The dietary supplements intended for use by infants and young children should have specific compositional legal requirements[5]. In several countries, dietary supplements do not generally require premarket review and approval by the Health ministry.

Although most commercially available probiotic strains are widely regarded as safe, there are significant concerns with respect to safety in particular populations.

There is a lack of exact information regarding the mechanisms through which probiotics act, correct administrative regimens and probiotic interactions. Much more research and investigation is needed in these areas. Also the properties of different probiotic species vary and can be strain-specific. So, the effects of one probiotic strain is not applicable to other probiotic strains , without proper research studies and confirmatory tests. Careful consideration should be given to these issues before patients are advised to use probiotic supplements in clinical practice.

Minor and Major risk factors

The Major risk factors for probiotic associated bacteremia and sepsis include immunosuppression, major dental surgical procedures [12] and prematurity in infants. Minor risk factors include the presence of a central venous catheter, impairment of the intestinal epithelial barrier (diarrheal diseases), pre existing cardiac valvular disease , prolonged antibiotic therapy with broad spectrum antibiotics to which the probiotic bacteria is resistant, probiotic administration to patients with active oral infections and also administration of probiotics via a jejunostomy tube is a risk factor as a large number of viable probiotic bacteria can by pass the acidity of the stomach and reach the intestine[19]. Probiotics therefore should be used cautiously in patients with such risk factors.

IV BACTEREMIA

The most important area of concern with probiotic use is the risk of bacteremia and sepsis. Bacteremia due to probiotics, is rare , but recently quite a number of cases have been reported.

Systemic infections associated with specific probiotics where sepsis or endocarditis with lactobacilli have been reported in isolated reports[12]. Bacteremia due to lactobacilli rarely occurs, but predisposing factors include immunosuppression, prior hospitalization, severe underlying comorbidities, previous antibiotic therapy, and prior surgical interventions can cause bacteremia. Although there have been infrequent reports of lactobacillemia and fungemia, there have been no reports of bifidobacterial sepsis associated with the use of a probiotic to date, due to the low pathogenicity of bifidobacteria species. However most cases of probiotic bacteremia respond well to antibiotic therapy.

Probiotics is now being used increasingly in dentistry as replacement therapy for replacing cariogenic bacteria with probiotic bacteria. It is known that transient bacteremia can occur during dental manipulations and surgical procedures. The incidence of bacteremia , due to various dental procedures such as flossing, scaling , root planning,rubber dam placement, endodontic treatment, periodontal surgery, tooth brushing,tooth extractions and water irrigation devices has been documented[7,18] . A major risk factor of use of probiotics in replacement therapy is whether such probiotic bacteria which replace part of the oral flora, can cause bacteremia during such dental procedures or dental manipulations when they enter the bloodstream[1] .

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It is important to consider the amount of disease activity and risk factors of a patient, like enteric infections or use of immunosuppressive therapies, before administering probiotic therapy.There are no large clinical studies that have shown a strong benefit from probiotic therapy in pediatric patients with Ulcerative Colitis. Although it has been proposed that probiotics can provide potential benefits in certain conditions, risks and benefits should still be carefully assessed before initiating this therapy in patients with UC, especially when they have severely active disease and may be immune compromised.

TABLE 1

Reported Cases of Bacteremia due to probiotic use

Name of author	Probiotic bacteria used	Risk factors
Elahen Vahabnezhad et al(5)	Lactobacillus rhamnosus	Ulcerative colitis
Robert J Boyle et al(19)	LGG, B.subtilis	Immunosuppression, infants
Land MH et al(10)	LGG, 10^{10} CFU/d	Cardiac surgery,antibiotic associated diarrhea
Kunz AN et al(9)	LGG	Prematurity, short gut syndrome
De Groote MA et al(4)	LGG ¼ capsule/d	Prematurity, CVC
Mackay AD et al(12)	Lactobacillus rhamnosus, $3x10^9$ CFU/d	Dental extractions, Mitral regurgitation
Oggioni MR et al(17)	Bacillus subtilis 10^9 spores/d	Chronic lymphocytic leukemia

V CONCLUSIONS

Probiotics marketed for specific health benefits require premarket review and should be approved and regulated by the health ministry of each country. Such case reports should alert the population to the possible risk of over the counter probiotic medications and products and the need for proper consultation of physicians, before using any probiotic containing product or medication.

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