Research Paper

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PROBIOTICS IN GASTROINTESTINAL INFECTIONS - AN OVERVIEW

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ABSTRACT Gastrointestinal infections are a major of morbidity and mortality worldwide, particularly in developing countries. The use of probiotics to prevent and treat a variety of diarrhoeal diseases has gained favour in recent years. Probiotics have been studied in a variety of gastrointestinal infections and are an appearing concept. Several placebo-controlled trials indicated that lactobacilli have a suppressive effect on Helicobactor pylori infection. Several placebo-controlled trials showed a reduction in the severity and duration of acute diarrheoa in children by use of Lactobacillus. Controlled trials support the use of Lactobacillus Sacchromyces boulardii for the prevention of acute diarrhoeal diseases (ADD). Studies of probiotics for the prevention of traveler's diarrheoa yield conflicting results; and their routine use cannot be recommended in this setting. We will discuss possible mechanisms by which probiotics could have a beneficial impact by enhancing the prevention or treatment of diarrhoeal diseases. However, the overall efficacy of these treatments and mechanisms by which probiotics ameliorate gastrointestinal infections are mostly unknown. Additional clinical trials are indicated to define the role of probiotics further before their wide-spread use can be recommended. This paper will review the recent literature relevant to the mechanism of action and utility of probiotics in the treatment of gastrointestinal infections.

KEYWORDS

Probiotics, Gastrointestinal Infections

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Introduction:

The concept of probiotics probably dates back to 1908, when noble prize winner Eli Metchnikoff suggested that the long life of Bulgarian peasants resulted from their consumption of fermented milk products1. The term “Probiotic” was first used in 1965 by Lilly and Stillwell for describing substances secreted by one organism which stimulate the growth of another2. Marteau et al,in 2002 defined them as “Microbial preparations or components of microbial cells that have a beneficial effect on health and well being.3.

The greatest concentration of commensal organisms is found in the gastrointestinal tract (GIT), which has been more than 400/m2 of surface area. This constitutes the second largest surface area of the body following that of the respiratory tract. The GIT harbors a rich flora of more than 500 different bacterial species; some of which have important health functions, which include stimulating the immune system, protecting the host from invading bacteria and viruses and aiding digestion,4, The gut flora is acquired rapidly after birth, remains relatively stable throughout the life and is essential for human homeostasis. When the intestinal micro flora is developing, the interaction of this micro flora with the host results in evolution of a unique and distinct intestinal immune system. The challenge facing this host mucosal immune system is to discriminate between pathogens and benign organisms by stimulating protective immunity without excessive inflammatory response that may disrupt the integrity of the GIT mucosa5.

The use of antibiotics, immunosuppressive therapy and irradiation, amongst other means of treatment, may cause alteration in the normal flora. At that phase introduction of beneficial species into the GIT can be a very attractive option to re-establish the microbial equilibrium and prevent disease6.

Various microbes most commonly used in the probiotic preparations include bacteria like Bifidobacterium, Enterococcus, Escherichia, Bacillus and Streptococcus and also some fungal strains belonging to the group Saccharomyces.

The micro organisms used in probiotic preparation should be recognized as safe. These should be resistant to bile, hydrochloric acid and pancreatic juice. These should have anti carcinogenic activity, stimulate immune system, have reduced intestinal permeability, produce lactic acid able to survive in acidic conditions of the duodenum7. Foods for human consumption that contain mainly lactic acid bacteria include fermented milks, cheeses, fruit juices, wine and sausages. Single and mixed cultures of live organisms are used in probiotic preparation8.

Mechanism of Action:

Several mechanisms have been postulated regarding action of probiotics. Partial lactose digestion and stimulation of the intestinal mucosal lactase activity has been postulated as a possible mechanism against some types of diarrhoeal diseases. Lactobacillus used in the fermented milk industry has active beta glactosidase to decrease the lactose concentration in dairy products, which may affect the severity of osmotic diarrhoea due to rota virus 9,10. Lactic acid bacteria produce several metabolites like free fatty acid, hydrogen peroxide and bacteriocins which prevent the growth of food borne pathogens in dairy products.11. Probiotics can also follow enzymatic mechanism to modify toxin receptors and block toxin mediated pathology12. Probiotic agents also prevent colonization of pathogens by competitive inhibtion13. Lactobacillus rhamonosus strain GG has proven beneficial affects on intestinal immunity. It increases number of immunoglobulin A secrseting cells in the intestinal mucosa. It also stimulates local release of infection. It facilitates antigen transport to underlying lymphoid cells which serve to increase antigen uptake in peyer's patches14.

Probiotics are live organisms and hence it is possible that these may result in infection in the host. The risk and morbidity of sepsis due to probiotic bacteria should be weighed against the potential for sepsis due to more pathological bacteria and the morbidity of diseases for which probiotic bacteria are being used as therapeutic agents. In future well designed placebo controlled studies with validated results are required for ascertaining the true health benefits of probiotics. The important point in this regard is careful selection of the probiotic agent, its dose standardization and a through knowledge of its beneficial effects.

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The term probiotic was derived from the greek word meaning "For Life"15. An expert panel commissioned by FAO (Food and Agriculture Organization) and WHO defined probiotic as "Live micro organisms", which when administered in adequate amount confers a health benefit on the host 16. Lactobacillus rhamonosus (LGG) was the first probiotic, which received most clinical attention to date17. The Lactobacillus strain used traditionally for fermentation in dairy industry was unable to implant the gut; so lactobacillus rhamnosus strain GG was discovered in 1985 that satisfied the ideal qualities for probiotics18. Lactobacillus rhamnosus strain GG has proven beneficial affects on intestinal immunity.

Probiotic is a non digestible food ingredient that confers benefits on host by selectively stimulating the growth and / or activity of one bacterium or a group of bacteria in colon, and thus improves the host health. Probiotics are dietary carbohydrates that escape digestion in the upper gastrointestinal tract, alter the bacterial composition of the gut by changing the type of the substrate provided to the existing microbial population in the gut e.g. fructooligosaccharides, glucooligosacchrides and inulin.In combination probiotics and prebiotics are syn-biotics. These improve the survival of bacteria in the GIT and thereby become more beneficial.

Uses of probiotics :

Probiotics have been shown to be effective in varied clinical conditions –ranging from infantile diarrhoea necrotizing enterocolitis, antibiotic associated diarrhoea, relapsing clostridium deficile colitis, helicobacter pylori infections, inflammatory bowel disease, females uro-genital infections and some carcinomas.

Probiotic effectiveness in various gastrointestinal ailments has been discussed under individual headings.

Diarrhoea:

Probiotics have preventive as well as curative effects on several types of diarrhoea of different etiologies. Prevention and therapy of diarrhoea have been successfully investigated for numerous dietary probiotic microorganism e.g. Lactobacillus rhamnosus GG,L.reuteri, certain strains of L.casei, L.acidophilus, Escherichia coli strains nissle 1917 and certain bifidobacteria and enterococci (Enterococcus faecium SF-68) as well the probiotic yeast Sacchromyces boulardii in regard to their medicinal use, either as single strain or as mixed culter probiotics19.

Various randomised, double blinded and placebo controlled studies on rota virus diarrhoea have shown beneficial effects with Acidobacillus rhamnosus strain GG and Bifidobacterium lactis BB-12 for prevention and Lactobacillus reuteri SD 2222 for treatment of acute diarrhoea caused by rota virus in children 20,21.

Antibiotic Associated Diarrhea:

Although newer antibiotics with a broad spectrum of activity and fewer side effects have been developed, the incidence of antibiotic associated diarrhoea (AAD) still ranges from 3.2-29/100 hospitalized patients22. The complications of AAD include electrolyte imbalance, dehydration, pseudomembran colitis and toxic mega colon. Antibiotics with a spectrum of activity against anaerobic bacteria have been associated with higher rates of AAD, although nearly all types of antibiotics have similar association. A Meta analysis to evaluate the efficacy of probiotics in prevention and treatment of AAD showed an odd ratio 0.30 (p-less then 0.001) in favour of active treatment over placebo with Sacccharomyces boulardii 14.

Traveller's Diarrhoea:

Travellers diarrhoea is a common health problem among travellers. Rates of travelser's diarhhoea can range from 5-50% depending upon destination23. A meta analysis was done on published randomized controlled clinical trials of traveller's diarrhoea cases. It was concluded that probiotic significantly prevent travelller's diarrhoea. The effects of probiotic strains in the prevention of diarrhoea caused by enterotoxinogenic microorganisms have been studied in subjects travelling to a number of destinations. Generally the pathogens have not been identified. Even though statistically significant differences between groups of individuals receiving active substance and placebo products have been achieved, the clinical effects have been moderate 24. Further, the same probiotic strains had variable effects depending on the travel destination of the subject. Saccromyces boulardii and a mixture of Lactobacillus acidophilics and Bifidobacterium bifidum had significant efficacy 35.

Inflammatory Bowel Disease

Inflammatory bowel disease classically includes ulcerative colitis and Chron's disease representing different pattern of chronic inflammation of GIT. Recent clinical experimental observation showed imbalance in the intestinal mucosa with relative predominance of aggressive bacteria and relative paucity of protective bacteria.26 and also stimulation of proinflammatory immunological mechanisms14.

Necrotizing Enterocolitis(NE)

Necrotizing Enterocolitis (NE) is one devastating intestinal disorder that a preterm infant may face in a Neonatal Intensive Care Unit (NICU). It is characterized by abdominal distension, bilious vomiting, bloody diarrhoea, lethargy, apnoea and bradycardia27. NE reported in 10 to 25% of preterm infants, admitted to NICU and may affect 1/3 to ½ of all low birth weight infants. The morality ranges from 20 to 30% and those who survive have long term sequelae as short gut syndrome, intestinal obstruction and multi-organ failure28. Low birth weight pre-term infants delivered by Caesarean section often require intensive care and are breast fed only after several days. The normal process by which organisms such as Lactobacillus species are ingested via vaginal birth and propagated by mother's milk does not take place in these infants29. Therefore these infants are exposed to a plethora of pathogenic microbes like Clostridium, Escherichia, Salmonella, Shigella, Campylobactor, Pseudomnas, Stretococcus, Enterococcus, Staphylococcus, which colonize the intestine and increase the risk of NE. Further, pre-term infants given formula feeding have less Lactobacillus and Bifidobacterium species in their stool compared to controls. These findings suggest a correlation between NE and Lactobacillus species. A human trial with 2.5 x 108 live Lactobacillus acidophilus and 2.5 x 108 live Bifidobacterium infantis given to 1,237 newborn in Columbia, resulted in 60% reduction in NE and overall mortality30. A correlation between normal gut microflora and protection against various infections has been reported. This supports the concept of early intestinal colonization with organisms such as Lactobacillus rhamnosus and Bifidobacterium infantis and subsequent protection against NE31.

Summary

The probiotic theory offers an intriguing approach to controlling negative metabolic or pathogenic activities of microbes to which we are exposed on a daily basis. Throughout the human life cycle, conditions exist that produce increased risks for infection, increased activity of opportunistic pathogens and decreased protection from normal micro flora. Old age, treatment with antibiotics and immunocompromised states can all contribute to disruption of colonizing microbes. When we consider the increased environmental threats of antibiotic resistant pathogens emerging new pathogens and serious sequelae of "treatable" infections; an intervention with essentially no risk that may provide another barrier to microbial assault is attractive. Probiotics could provide this benefit. Dietary rather than drug interventions have obvious advantages in term of cost required to characterize health benefits further and to define the "active principle" in probiotic preparations.

Conclusion

Probiotic therapy has already made its way in the treatment of number of gastrointestinal conditions that may be infectious, inflammatory, neoplastic and allergic. There is a long list of potentials of giving probiotics in a number of these conditions. But before bringing

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probiotics into routine usage, proper evaluation of these products is essential. Several important criteria and standards regarding quality and reliability have to be met with. Thus future well designed placebo controlled studies with validated resulted are required for ascertaining the true health benefits of these products. The important approach includes careful selection of the probiotic agent, its dose standardization and a thorough knowledge of its beneficial effects over and above the toxic effects; so that this traditional therapy proves to be an effective tool in medical field.

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