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Are Probiotics Safe Enough to Become Available Universally?

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Abstract

Objective: To critically analyze the essentiality and irrational zinc preparations available in Indian market.

Widespread use of probiotics and the presence of these microorganisms in human food-chain established an argument against the safety profile of probiotics. Various case-reports, clinical trials, and experimental studies have mentioned different types of side effects induced by the consumption of probiotics. Although previous studies reported beneficial impacts in alleviating the gastrointestinal (GI) problems, cardiovascular disorders, and metabolic syndromes, the most at-risk groups of populations such as pediatrics, geriatrics, critically-ill patients are at higher risks of the occurrence of some life-threatening or life-lasting adverse events. Bacteremia, fungemia, GI disorders, metabolic problems, extreme immune stimulations, seizure, Kawasaki disease, etc. have been associated with the use of probiotics. Moreover, due to the antibiotic resistance gene reservoir property of the GI tract, transference of the resistance genes among probiotics, normal human flora, and pathogenic microorganisms endow probiotics to propagate antibiotic resistance genes globally.

Keywords: Probiotics; Adverse effect; Safety; Side effect; Microbiota

Introduction

With increased knowledge of the impact of normal flora on human health, the focus of the last decade's studies has been given to the maintenance of gut microbiota [1]. Restitution of the imbalanced microorganisms in oral, vaginal, and rectal cavities, in the intestine and on the skin through living microorganisms available in pharmaceutical preparations and food, demonstrated beneficial influences on human health [2]. According to the definition of world health organization (WHO), "probiotics are living microorganisms which might have beneficial influences on human health in adequate amounts." The widespread use of probiotics and lack of knowledge about the exact mechanism of these microorganisms created a doubt on the safety profile of probiotics [3,4].

Previous studies showed that probiotics might be helpful in the management and symptom alleviation of various disorders. Probiotics are frequently useful in symptom improvements of the gastrointestinal tract (GIT) such as diarrhea, constipation, irritable bowel syndrome (IBS), and inflammatory bowel disease (IBD). Moreover, respiratory inflammations, hyperlipidemia, and metabolic syndromes have been alleviated through the consumption of probiotics [5].

Various case reports, animal studies, and clinical trials reported different kinds of adverse events as the side-effect of probiotic consumption. Infants, elderly, critically ill patients, and immunocompromised patients are among the high-risk populations which showed various life- lasting and life-threatening adverse events. However, the strain of the microorganism and diet of the patient demonstrated an essential role in the prevalence of adverse effects [6].

Adverse Effects, From Mild to Severe Types

GIT disorders

Abdominal pain, diarrhea, constipation, bloating, vomiting, flatulence, loss of appetite, and taste distribution are the most frequently reported adverse effect of probiotics [6]. Consumption of lactobacillus strains is associated with the occurrence of diarrhea and softer stools. Moreover, chronic consumption of probiotics induces stomach related events such as bloating and flatulence [7]. Although most of the GIT disorders are mild, a clinical trial reported eight deaths out of 9 patients with intestinal ischemia following the consumption of Bifidobacterium and Lactobacillus strains [8].

Skin adverse events

Dry skin, acne and rash are among the skin adverse effects associated with the consumption of probiotics [9]. Although skin rashes might be indicative of toxin elimination from the body, variation of the skin normal flora through consumption of probiotics plays an important role in the prevalence of adverse skin events [6,9].

Metabolic disorders and obesity

Deconjugation of bile salts through probiotics results in the production of D-lactic and brings acidosis for the patient. Moreover, despite the investigations about the beneficial impact of probiotics in the management of obesity, recent studies proved a controversial impact in some patients; therefore, an argument about the role of probiotics in the management of obesity has been established [10,11].

Infection

Among Lactobacillus spp. consumers, bacteremia was the most frequently observed side-effect. However, Lactobacillus rhamnosus plays the most crucial role in the prevalence of bacteremia [12]. Increasing the pH of the intestine through the production of peptides and short-chain fatty acids (SCFA) and occupying available niches of the intestine by pathogenic microorganisms facilitate the prevalence of bacteremia in probiotic consumers [13].

Saccharomyces species (boulardii and cerevisiae), which are frequently used for discontinuing antibiotic-associated diarrhea (ADD), lead to fungemia in critically ill patients [14].

Sepsis and entrance of these microorganisms into the blood have a confirmed relationship with the consumption of probiotics [13,14].

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Immune stimulation

The occurrence of autoimmune diseases has been associated with the consumption of probiotics in some patients. The influence of probiotics in both adaptive and intrinsic immune systems generated global concern regarding the secretion of cytokines and activation of dendritic cells [15]. Although human studies did not report harmful effects, animal studies confirmed the impact of probiotics on nuclear factor κb and Jun Nterminal kinase [16].

Antibiotic resistance propagation

After the discovery of the exact mechanism of transferring antibiotic resistance genes among different microorganisms, the role of probiotics in the transference of genetic elements containing antimicrobial resistance genes obtained careful attention from various studies [17]. Transference of genetic elements containing resistance elements depends widely on the capability of microorganisms for delivering and receiving the genes. Also, the size of the genetic elements plays an important role in the probability of the gene transference; plasmids and mobile genetic elements are the most probable transmitters [18]. However, the chromosomal mutation can be rarely transferred through mobile elements containing vancomycin resistance genes [19].

Transference of the resistance genes carried by probiotics to the normal flora and pathogenic microorganisms present in the gut in infectious situations results in propagating resistance genes among a wide range of microorganisms [20].

Notably, different species among probiotics (even bacteria or yeast) might be able to transfer specific antibiotic resistance genes. To illustrate, vancomycin and tetracycline resistance genes are frequently transferred through Lactobacillus species [21]. Also, Bifidobacterium species have a significant role in the prevalence of resistance toward streptomycin and mupirocin [22].

Conclusion

DDespite the health benefits associated with the consumption of probiotics, inappropriate use of probiotics, especially in high-risk populations, might induce various health implications. Furthermore, receiving enough fluid, decreasing the dose of the microorganisms, and UV radiation showed healthful impacts in the management of the adverse effects.

Due to the dependency of gene elements carried by microorganisms to the probiotic source, it is essential to consider the source of extraction as an effective factor. Obesity and type 2 diabetes have been observed in the newborn mouse, as the result of breast-feeding from an obese and diabetic mother.

This brief review aimed to clarify that the public assumption about probiotics is not well-founded, and further clinical trials are needed to support the idea of limiting worldwide use of probiotics.

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