ARE PROBIOTICS HELPFUL FOR ALLERGIES?

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ABSTRACTS

A hypersensitive reaction brought on by the body's immune system reacting to a particular antigen is called an allergy. Over the past few decades, allergy illness prevalence has significantly increased, particularly in Western countries. According to the hygiene hypothesis, a child's vulnerability to allergies may rise if they have less early exposure to microorganisms and/or parasites. Efforts to balance immune function using probiotics have been driven by the important function that the microbiota plays in the interaction between the human immune system and its environment. Research on the advantages of using probiotics to prevent or lessen allergy symptoms has significantly increased in the last few years. This paper discusses the safety of using probiotics as well as their potential to prevent or lessen allergy illnesses.

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INTRODUCTION

Worldwide, the prevalence of allergy illnesses is sharply rising in developed as well as developing countries. Asthma, rhinitis, anaphylaxis, medication allergy, food and insect allergy, eczema, urticaria (hives), and angioedema are among the allergic illnesses. Children are primarily affected by the rising incidence of allergies during the past 20 years.[1] When comparing data from the early 1980s to the beginning of the 21st century, the overall number of patients with bronchial asthma in the United States increased by 60%. In the meantime, the study population's incidence of allergic rhinitis varied from 9% to 42%. The prevalence of allergies is highest in the under-18 age group, with 5.4% having food allergies, 10% having allergic rhinitis, 41% having asthma, and 11.6% having atopic dermatitis.[2]

Terminology

The definition of allergy is a hypersensitivity reaction brought on by the immune system's reaction to certain antigens known as allergens. Allergies to particular foods, house dust, pollen, mites, animal dander, or other substances; usually caused by immunoglobulin (Ig) E. After these allergens interact with innate immune cells, an immunological cascade occurs that produces allergen-specific IgE, sensitizes effector cells, and biases adaptive immunity toward T helper 2 (Th2). Frequent exposure to the allergen causes mast cell and basophil activation, which is followed by the production of allergy mediators and a range of symptoms, from itchy skin rashes and sneezing to severe dyspnea and anaphylactic reactions.[3]

The Hygiene Hypothesis

The prevalence of allergies and asthma has sharply increased worldwide in the last several decades. This growth has primarily occurred in wealthier or Western countries, although similar increases have also occurred in low-income countries. There is a stark contrast between the rise in allergies and asthma and the fall in the prevalence of infectious diseases. The "hygiene hypothesis," which connects microbial exposure in children in affluent nations with decreased immune system stimulation and Th1/Th2 imbalance, predisposes to allergy disorders, explains the current rising occurrence of allergic diseases.[4,5,6]

According to the hygiene hypothesis, early childhood exposure to lesser bacterial illnesses, microbiota in the gut, and parasites may enhance the probability of acquiring allergy disorders. This theory also takes into account decreases in infectious diseases generated by improved public health efforts, medical technology

advancements, vaccination campaigns, and hygiene activities. Evidence linking population density, sanitary conditions, and bigger family sizes with a decreased prevalence of allergy illnesses like eczema, hay fever, and asthma first gave rise to the phrase "hygiene hypothesis." This hypothesis proposed that infection might protect against allergies. [4,5,7]

Gut Immune System

The immune system can balance systemic tolerance and protective mucosal immunity levels in a healthy gut. As the connection between the gut microbiota, luminal antigens, and the epithelial barrier is established, immune homeostasis in the gut grows. After delivery, the sterile newborn's gut is gradually colonized by bacteria from the surrounding and mother's gut flora, as well as potentially by genetic effects. This process is known as microbial colonization of the gut. Early-life exposure to microbial flora can alter the Th1/Th2 cytokine balance in favor of the Th1 cell response.[8,9]

During the early stages of life, a child's immune system develops primarily in a Th2 manner, while as they mature postnatally, they gradually exhibit increasing Th1 affinity and Th2 inhibition. Therefore, to stop the onset of childhood allergy disorders, the immature Th2-dominated neonatal response needs to undergo environmental maturation by contact with bacteria in the early postnatal period. If this isn't the case, the baby's immune system will polarize toward a Th2 phenotype from a young age.[8,10] Reduced exposure to microbes during infancy is closely linked to an increase in allergy disorders. The gut microbiota is the body's greatest exposure to microbes and has a role in stimulating the immune system.[8]

Today, with greater antibiotic use, higher consumption of sterile foods, smaller family sizes, and the Western lifestyle's excessive sanitation, all of these will result in lower childhood infection rates, leading to a rise in allergy sickness.[10,11,12] The importance of the microbiota's interaction with the human immune system promotes efforts to improve immune function by administering helpful live microorganisms (bacteria), known as probiotics.[5]

What are Probiotics?

Probiotics are defined by the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) as 'living microorganisms' that provide health advantages to their hosts when consumed in sufficient quantities.[13] Simply said, probiotics are live, ingested microorganisms that can modify the gut microbial community in a beneficial way for their host.[10] The term probiotic means

'for life' and is currently used to refer to bacteria that have been linked to health benefits in humans and animals.[13]

The following are some widely acknowledged traits of probiotic bacteria:

- Microbiological organisms
- Remain viable and stable throughout cultivation, modification, and storage before utilization.
- Not harmed by the pancreatic, bile, or stomach's digesting processes.
- Able to induce a host response when it enters the microbiome of the gut
- When ingested, provides functional or health benefits to its host.[10,13]

In addition to having to be resistant to bile and stomach acid to survive passage through the gastrointestinal tract, probiotics that are used in meals, nutritional supplements, or as active ingredients in approved medications also must have the ability to multiply in the gut.[14]

Based on their mode of action, the advantages of probiotics for humans can be categorized into four groups: immunological, physiological, nutritional, and microbiological. Within their microbiological role, probiotics stop pathogenic microorganisms from attaching to or invading the host body. Probiotics occupy the region or living habitat of pathogenic agents or directly oppose them by creating bacteriostatic or bactericidal compounds. Certain probiotics can synthesize several advantageous nutrients for the body, including biotin, folate, nicotinic acid, and thiamine. Probiotics have also been shown to affect physiology and benefit the host. For instance, they have been shown to enhance ion absorption by gastrointestinal epithelial cells and lessen bile salt-induced toxicity.[14,15]

Different kinds of probiotics provide various functions, and the advantages to human health have mostly been established for select types of probiotics. Lactobacillus, Bifidobacterium, Bacillus, Pediococcus, and some yeasts are among the genera that are utilized as probiotics. The most common lactic acid bacteria (LAB) species utilized in food and feed fermentation as well as probiotic production is the genus Lactobacillus.[16,17,18]

Probiotics are regarded as functional nutrients that help repair the gut's symbiotic microbiota. Most probiotics are bacteria that are identical to those found naturally in the human gut, particularly in breastfed newborns and are recognized to offer inherent preventive characteristics against a variety of illnesses. The two groups of bacteria that are most common are Lactobacillus and Bifidobacterium. Different species—such as Bifidobacterium bifidus, Lactobacillus acidophilus, and others with varying strains—are involved in each group. Some common probiotics, such as

Saccharomyces boulardii, are yeasts. A few types of bacteria found in probiotic formulations are Bifidobacterium bifidum, Bifidobacteria longum, Bifidobacteria infantis, Streptococcus thermophilus, Lactobacillus acidophilus, Lactobacillus rhamnosus, Lactobacillus bulgaricus, Lactobacillus salivarius, Lactobacillus plantarum, Lactobacillus casei, Lactobacillus sporogenes, and Homeostatic Soil Organisms (HSO's).[18]

The Way Probiotics Work in Allergies

Allergic diseases are systemic illnesses caused by immune system dysfunction. Several allergic illnesses, including allergic rhinitis, allergic asthma, atopic dermatitis, and food allergy, are caused by a complex combination of hereditary and environmental variables.[19] According to the hygiene hypothesis, allergies and associated illnesses may arise as a result of inadequate or abnormal exposure to environmental microorganisms.[4] As previously noted, allergic illnesses are related to a shift in the Th1/Th2 cytokine balance, leading to Th2 cytokine overactivation and the release of interleukin-4 (IL-4), IL-5, and IL-13, as well as IgE formation. Probiotic therapy has a significant impact on the gut milieu by altering local microbiota and cytokine release, as well as potentially influencing Toll-like receptors and enterocyte proteoglycan recognition proteins, which contribute to dendritic cell activation and Th1 responses. The subsequent activation of Th1 cytokines has the potential to inhibit Th2 responses.[8]

By altering the gut microbiota's composition, probiotics support dendritic cell migration and maturation. Dendritic cells in gut lymphoid tissue can stimulate the production of peripheral T regulatory (Treg) cells, which play an important role in immune system homeostasis. Tregs maintain Th1 and Th2 cells in balance, along with anti- and pro-allergic cytokines.[20] Probiotics can also stimulate mucosal IgA levels and allergen-specific B and T cell responses, making them useful for treating allergic disorders.[8,21,22]

Another way probiotics influence the composition of the gut microbiota. Supplementation with probiotic bacteria such as Lactobacillus rhamnosus GG (LGG) or L. casei can alter the gut microbiota of allergic children by reducing pathogenic bacteria such as clostridia while raising or maintaining the number of beneficial bifidobacteria.[22,23] This is mostly accomplished by changing the intestinal lumen's environment by reducing pH levels and nutrient competition, which will produce physiological conditions that prevent the growth of harmful bacteria.[24]

Probiotics' capacity to decrease inflammatory cytokines and raise intestinal

permeability in vitro has sparked interest in their potential benefits for allergies. Such effects are desirable for treating allergic diseases. As a result, numerous research has been created to investigate the effectiveness of probiotics in treating a variety of allergic disorders, including atopic dermatitis, allergic rhinitis, asthma, and food allergies.[9]

Role of Probiotics in Atopic Dermatitis

Atopic dermatitis (AD) is the most prevalent family, chronic, recurrent, and noncommunicable inflammatory skin disease, with a wide clinical spectrum.[25] There has been conflicting evidence on the efficacy of probiotics as a treatment for atopic dermatitis. While some research has demonstrated an apparent impact of probiotics in symptom reduction, other investigations have not found any evident benefit.[15]

Yesilova et al. treated children with atopic dermatitis with Bifidobacterium bifidum, Lactobacillus acidophilus, Lactobacillus casei, and Lactobacillus salivarius for 8 weeks, resulting in decreased symptoms, serum IgE, IL-5, IL-6, and interferon γ levels significantly lower than the placebo group.[26] Weston et al. gave Lactobacillus fermentum VRI-003 PCC to children with atopic dermatitis aged 6 to 18 months for eight weeks. When compared to the placebo group, the probiotic group experienced a substantial reduction in atopic dermatitis symptoms as measured by the SCORAD at 16 weeks.[27]

Despite the benefits of probiotics in treating allergic illnesses, not all research has found the same results. Giving Lactobacillus acidophilus to newborns whose moms had a history of allergies during the first six months of life did not lower the infant population's risk of sensitization or atopic dermatitis, according to Taylor AL and colleagues.[28]

Role of Probiotics in Allergic Rhinitis

Allergic rhinitis frequently lowers patients' quality of life and diminishes work effectiveness. When used to treat allergic rhinitis, conventional antiallergic medications might have side effects such as tiredness, drowsiness, and dry mouth, among others, which can lower the patient's quality of life. Consequently, it's essential to look for other treatments. According to several current studies, probiotics with anti-allergic properties should help lessen the symptoms of allergic rhinitis. Previous research has shown that probiotics can have a variety of impacts, including a reduction in Th2 cell inflammatory factors and/or an increase in Th1 cell factors, changes in allergy-related immunoglobulins and cell migration, regulation of the Th1/Th2 balance, and gut microbiota restoration.[29]

According to Giovannini et al., giving fermented milk containing Lactobacillus casei to 64 preschoolers between the ages of 2 and 5 for a whole year decreased the frequency of allergic rhinitis episodes.[30] Shabestari MS et al. administered probiotic capsules comprising Lactobacillus casei, L. acidophilus, L. rhamnosus, L. bulgaricus, Bifidobacterium breve, B. longum, Streptococcus thermophilus, Fructooligosaccharides to 60 individuals over the age of 15 for 8 weeks. 14.3% of patients with sneeze (allergic rhinitis) at baseline in the probiotic group saw a significant decrease in symptoms, which reduced to 4.6%. Furthermore, following probiotic treatment, the probiotic group required fewer oral and nasal corticosteroids than the control group.[31]

Role of Probiotics in Bronchial Asthma

Asthma is a complex condition characterized by chronic inflammation of the respiratory tract, reversible airflow limitation, and bronchial hyperresponsiveness.[32,33] Probiotics interact with intestinal epithelial cells (IECs) and immunocompetent cells in the lamina propria via Toll-like receptors after being administered orally. The cytokines, chemokines, and mediators are produced in response to this interaction. Furthermore, probiotics stimulate T regulatory cells to release IL-10, a key anti-inflammatory and regulatory cytokine. Additionally, probiotics modify the gut microbiota, prevent harmful bacteria from proliferating in the intestines, encourage the development of Th1 responses, decrease the synthesis of IgE, lessen inflammation in the airways, and strengthen the body's defenses against respiratory infections.[34]

The Probiotics in Pediatric Asthma Management (PROPAM) trial gave probiotics comprising Ligilactobacillus salivarius LS01 (DSM 22775) and Bifidobacterium breve B632 (DSM 24706) to 422 asthmatic children aged 3-14 years for 12 weeks. The frequency of asthma relapses was decreased by over a third and the number of asthma exacerbations was dramatically decreased by this probiotic mix.[35] Giudice MMD et al administered a Bifidobacteria mixture containing Bifidobacterium longum BB536, Bifidobacterium infantis M-63, and Bifidobacterium breve M-16 V to children aged 9 ± 2.2 years for 4 weeks. The results significantly reduced respiratory symptoms and improved quality of life (QoL), while the placebo group experienced worsening symptoms and QoL.[36]

Role of Probiotics in Food Allergy

Food allergy is an aberrant immunological response caused by the intake of allergens in food or food additives. This reaction can be IgE

(immunoglobulin E) mediated or non-IgE mediated.[37,38] In Western countries, it affects 2% of adults and 8% of young children, and like other allergy illnesses, its prevalence is rising.[39]

Early in life, the immune system is underdeveloped and requires environmental stimuli, such as microbial exposure, to mature appropriately. The gut microbiota's composition varies during infancy before the onset of allergy illness, indicating a potential role for the gut microbiota in enhancing tolerance to harmless antigens. The gut microbiome responds to food allergies in two ways. On the one hand, intestinal epithelial cells are directly impacted by the gut microbiota. According to several studies, the gut microbiota may interact with macrophages and dendritic cells to release IL-22 and strengthen the connections between IECs. In addition, substances made by the gut microbiota, namely short-chain fatty acids (SCFA), may supply the energy needed for IEC growth and repair. On the other hand, the gut microbiota may control the development of T cells to preserve the balance between Th1/Th2 and Treg/Th17, which in turn controls the host immune system.[40,41,42]

Probiotic administration might theoretically be used to directly improve the host's gut microbiota. Studies indicate that probiotics, like Lactobacillus and Bifidobacterium, are effective metabolites in reducing the symptoms of food allergies. By colonizing the human gut and producing like SCFA to maintain the stability of the gut environment, probiotics can help maintain the balance of gut microbiota and avoid food allergies.[40,43]

Dewanty et al. found that administering Lactobacillus rhamnosus GG to children under 24 months with food allergies, such as cow's milk, eggs, peanuts, carrots, and apples, can diminish atopy symptoms and decrease the SCORAD index.[44] Canani et al. found that 220 children who received Extensively Hydrolyzed Casein Formula (EHCF) + Lactobacillus rhamnosus GG (LGG) developed faster tolerance to cow's milk allergy than those who received EHCF alone.[45]

Safety of Probiotics

For many years, probiotics have been utilized in food and dairy products without any adverse reactions. They are now being used more frequently to prevent, decrease, or treat various disorders, including allergies.[46] Despite being quite safe, probiotics might cause modest adverse effects in certain individuals, which normally go away on their own. Bloating, stomach gas, diarrhea, constipation, nausea, thirst, headaches and migraines, and skin responses are among the common side

effects of probiotics. Mild gastrointestinal problems (such as gas and bloating) normally resolve within a few weeks. When taking yeast probiotics, some people feel thirstier, especially during the first week.[17,47,48] In addition to adverse effects, Lactobacillus and bifidobacterium supplementation may increase the risk of bacteremia and sepsis, particularly in patients with impaired immune systems.[49,50,51,52]

Probiotic supplements should be taken with caution in high-risk individuals, such as those on:

- Anti-rejection medication after a stem cell or solid organ transplant.
- Individuals receiving immunosuppressive or corticosteroid medication, chemotherapy for cancer, and those with autoimmune illnesses.
- Individuals with structural heart disease, including valve defects or replacement, or a history of infective endocarditis.
- Individuals with acute abdomen, active bowel disease (e.g., colitis), neutropenia from chemotherapy or radiotherapy, or active intestine perforation/leakage.[46]

CONCLUSION

The prevalence of allergy disorders is rapidly growing in both developed and developing countries. Reduced baseline microbial exposure is highly correlated with the sharp rise in allergies. The important role of the interaction between microbiota and the human immune system encourages efforts to balance the development of the immune system by providing beneficial live microorganisms, namely probiotics. Studies indicate that probiotics can help prevent or lessen allergic reactions, including atopic dermatitis, allergic rhinitis, asthma, and food allergies. However, as other studies have not found any appreciable benefits, further research is required to fully understand the benefits of probiotics. Future research may examine the best probiotics to use, the best probiotic combinations to use, the dosage, the length of time they are administered, and whether they should be used throughout pregnancy, just after delivery, or exclusively in children or adults.

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