

Treatment of Allergic Rhinitis with Probiotics: An Alternative Approach

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Abstract

Allergic rhinitis is a skewed immune reaction to common antigens in the nasal mucosa; current therapy is not satisfactory and can cause a variety of complications. In recent decades, the incidence of allergic rhinitis is increasing every year. Published studies indicate that probiotics are beneficial in treating allergic rhinitis. This review aims to help in understanding the role of probiotics in the treatment of allergic rhinitis. We referred to the PubMed database as data source. This review focuses on the following aspects: The types of probiotics using in the treatment of allergic rhinitis, approaches of administration, its safety, mechanisms of action, treating results, and the perspectives to improve effectiveness of probiotics in the treatment of allergic rhinitis. This review reports the recent findings regarding the role of probiotics in the treatment of allergic rhinitis. Probiotics are a useful therapeutic remedy in the treatment of allergic rhinitis, but its underlying mechanisms remain to be further investigated.

Keywords: Allergy rhinitis, Bacteria, Mechanism, Probiotics, Theurapeutics

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Introduction

Allergic rhinitis is an allergic inflammation of the nasal airways with a rapidly increased prevalence in the past decades.^[1] Data show that up to 30% of the general population in the developed countries suffers from one or more atopic disease such as allergic rhinitis, asthma, and atopic dermatitis. Almost 3% of all the general practitioner consultations are for allergic rhinitis in the United Kingdom.^[2] While there are still no acceptable treatments for allergic rhinitis, the only remedy is to avoid contacting with the allergen or medications for controlling symptoms.^[3] The beneficial effect of probiotics has been demonstrated in the treatment of allergic diseases. One of the most important aspects of the beneficial effect to the host organism is that the probiotics can interact with the host immune system and

may modify the natural course of the allergic disease,^[4] while how probiotics may influence the immune system remains unclear. Studies indicated that probiotics are a profitable therapeutic treatment of allergic rhinitis.^[5] This review highlights the most recent findings regarding the important role of probiotics in the treatment of allergic rhinitis.

The types of probiotics using in the treatment of allergic rhinitis

Only a single probiotic strain was intensively involved in the studies of the treatment of most of allergic rhinitis, such as *Lactobacillus acidophilus*,^[5] *Lactobacillus paracasei*,^[6-9] *Lactobacillus casei*,^[10-12] *Lactobacillus rhamnosus*,^[13,14] *Bifidobacterium longum*,^[15-18] *Lactobacillus johnsonii* EM1,^[19] *Lactobacillus gasseri*,^[20,21] *Bacillus clausii*,^[22] *Escherichia coli* Nissle (EcN) 1917.^[23] However, recent studies have been starting to evaluate the treatment effect by using more than one strain of probiotics. For example, *Lactobacillus* GG (LGG) and *L. gasseri* were used in the treatment of allergic rhinitis,^[24] and the combined treatment effect of *L. acidophilus* and *Bifidobacterium lactis* were also determined.^[25] A probiotic mixture VSL#3 (VSL Pharmaceuticals, Fort Lauderdale, FL), which contains eight different probiotic strains (4 *lactobacilli*,

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3 *bifidobacteria*, and 1 *Streptococcus thermophilus*) were used in their study.^[26] Review of literatures revealed that *Lactobacillus* and *Bifidobacterium* were the most popular probiotics studied by researchers. Meijerink *et al.* suggested that the 28 strains of *Lactobacillus* and *Bifidobacterium* are the best choice for research purposes, as they have been isolated from different commercially available products, and being screened for their immunomodulatory properties in a coculture assay with human peripheral blood mononuclear cells.^[27]

Safety of probiotics in the treatment of allergic rhinitis

Probiotics means 'for life' and is defined by the World Health Organization (WHO) and the Food and Agriculture Organization (FAO) of the United Nations as 'live microorganisms which, when administered in adequate amounts as part of food, confers a beneficial health effect by producing gut microflora on the host'.^[28] Although, there are no adverse reactions reported in the treatment of allergic rhinitis; however, concerns regarding the safety of probiotics were raised by the outcomes of several clinical trials. For example, a mixture of six probiotic bacteria (*L. acidophilus*, *L. casei*, *L. salivarius*, *L. lactis*, *B. bifidum*, and *B. infantis*) suppressed the growth of most pathogens that caused pancreatitis complications in the preclinical animal studies,^[29] while this bacterial mixture that was used in the treatment of patients with severe acute pancreatitis could increase the patient's mortality rate.^[30] In addition, others reported that bacteremia and fungemia would be developed in ill patients and immunodeficient individuals after using probiotic bacteria.^[31] Probiotics might also cause sepsis in immunocompromised populations. Septicaemia in two children with short bowel syndrome was reported who have received LGG supplementation.^[32] Premature infants, children with abnormal immune function, immunocompromised hosts, and autoimmune disorders should avoid using these products.^[33] Other studies reported that *L. reuteri* and *L. plantarum* have been found to carry antibiotic resistance genes, so there is another possible risk of probiotics that it may transfer such genes to the host.^[34] There are also some other side effects of probiotics reported, such as, an increased rate of recurrent wheezing episodes,^[35] an augmented rate of atopic disorders,^[36] increased sensitization to allergens,^[37] adverse gastrointestinal symptoms, diarrhoea, due to heat-inactivated LGG supplementation. Thus, future clinical trials using probiotics should be accompanied by safety monitoring.

Route of administration in the treatment of allergic rhinitis

Oral administration of the probiotics is the routine way of treating diseases, for there are several generally

accepted characteristics of probiotics: (1) they are microbial organisms; (2) they can survive under gastric, biliary, and pancreatic digestion; and (3) probiotics are able to induce a host response once they enter the intestinal microbial ecosystem and yield a functional or clinical benefit to the host.^[28] A recent study showed that intraperitoneal delivery of *EcN* together with Ovalbumin (OVA)/Alum strongly inhibited the generation of OVA-induced Th2 responses. But applying *EcN* intranasal or orally did not reduce the allergic response.^[23] Other studies reported that the intranasal route with *VSL#3* had the capability to prevent the development of an allergic response in inhalant allergy model and oral therapy treatment with *VSL#3* was able to significantly reduce both systemic and local anaphylactic symptoms in food allergy model.^[23]

Mechanism of probiotics in the treatment of allergic rhinitis

The mechanism of action of probiotics is multi-faceted, and every probiotic may have its own pathways in affecting the host.^[38] Recent data indicated that probiotics could modulate the production of cytokines by monocytes and lymphocytes. In a study that 31 adult volunteers with allergic rhinitis orally received *Lactobacillus paracasei* ST11 for 8 weeks. The results showed that *Lactobacillus* downregulated systemic immune markers interleukin (IL)-5, IL-8, and IL-10 from the peripheral blood mononuclear cells.^[9] Decreased eosinophils and diminished interferon-gamma (IFN- γ) in peripheral blood was reported after the ingestion of *B. longum*, thus also reducing the need for medication in Japanese cedar pollinosis. They suggest that *B. longum* probably works by playing a regulatory effect on Th2 balance in allergic rhinitis.^[38] In a recent study, it was reported that *LGG* and *L. gasseri* were able to at least partly down-regulate the human Th2 immune response.^[38] With regard to asthmatic children with allergic rhinitis, the use of probiotics resulted in a significant reduction of the TNF- α , IFN- γ , IL-12, and IL-13 produced by the peripheral blood mononuclear cells. Therefore, this may suggest that probiotic supplementation has a clinical benefit for children suffering from allergic airway diseases such as asthma and allergic rhinitis.^[38] Another study demonstrates for the first time the ability of *Lactobacillus casei Shirota* to down-regulate both T-helper (Th)1- and Th2-type cytokines and to beneficially alter the balance of pollen-specific IgG and IgE levels in seasonal allergic rhinitis. These data show that probiotic supplementation modulates immune responses in allergic rhinitis and may have a potential to alleviate the severity of symptoms.^[38] Many studies have shown that allergic rhinitis is characterized by Th2 polarization with an elevated level of Th2-derived cytokines, including IL-4, IL-5, and IL-13.^[38]

It should also be noted that the efficacy might be probiotic specific. Although, probiotics can exert beneficial effects on the host through distinct cellular and molecular pathways, these mechanisms of action may vary from one kind of probiotic to another for the same immune response and may be regulated by a combination of several events. Thus making probiotics' mechanism of action a challenging, complex, and fertile area for investigation.

Therapeutic results of allergic rhinitis with probiotics

Recently, data from several published randomized double-blind, placebo-controlled trials showed that probiotics had a treatment effect on allergic rhinitis.^[6-9,13,14,24] Furthermore, other studies figured out that the ingestion of probiotics resulted in a reduction of symptoms in children and adults with allergic rhinitis by reducing the allergic response to house dust mite.^[5] Published studies also demonstrated that *L. casei* reduced the number of rhinitis episodes in 64 preschool children with allergic rhinitis.^[10] Nevertheless, these results have been questioned recently by another trial that showed patients treated with *LGG* during the birch-pollen season that were allergic to birch pollen and apple food had neither reduction of symptom score, nor of sensitization to birch pollen and apple after probiotics supplementation.^[14] These indicate that probiotics may be beneficial in the prevention and treatment of allergic rhinitis, but the therapeutic effect remains to be further investigated.

Novel approaches to improve effectiveness of probiotics in the treatment of allergic rhinitis

Hitherto, few studies have provided strong evidence showing that probiotics have an exact treatment effect on allergic disease. Many novel approaches to improve the treatment effect of probiotics on allergic rhinitis were done. Some studies focus on finding the exact effective strains, others are trying to use mixed strains to improve efficacy.^[6-9] Route of administration was also changed in the treatment of allergic rhinitis in some studies.^[23] Recently, *LGG*, IL-2, and green fluorescent protein (GFP) as a fusion protein (*LGG-IL-2-GFP*) were used to examine the bacterial uptake and the immune response induced by oral immunization, the result shows that *LGG* expressing an antigen could produce an effective immune response to the antigen and IL-2 can improve the response by increasing *LGG* expressing antigen survival in immune cells.^[39]

Conclusion

Probiotics may have an important role in the prevention and treatment of allergic rhinitis. The clinical benefit of probiotic therapy depends on numerous factors, such as type of bacterium, route of administration, dosing,

regimen, and other underlying host factors. Furthermore, selection of the most beneficial probiotic strain and the timing of supplementation still need to be determined. A fusion protein of probiotics may be a novel approach to improve effectiveness in the treatment of allergic rhinitis. Further studies should also clarify the clinical efficacy of probiotics, protocol of selecting, designing of appropriate study populations, and safety of using probiotics. Mechanisms of action of probiotics modulating immune response are also needed to be further elucidated.

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