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Probiotic Usage in Food Allergy Atopic Dermatitis Children. A Literature Review

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A B S T R A C T

Food allergy is a health problem that commonly occurs among children. One of the clinical manifestations of food allergy is atopic dermatitis. Atopic dermatitis (AD) is related to the immune system. The immune system is affected by intestinal microbes. Probiotics are substances that can regulate the immune system for the digestive tract, particularly in the intestines. Probiotics has a therapeutic effect on several illnesses, specifically those related to the immune system. The aimed of this review was to discuss knowledge related to the usage of probiotics for the therapy of atopic dermatitis caused by food allergies in children. This literature review focused on the mechanism of probiotics in children with atopic dermatitis caused by food allergy. We use the journal article related to probiotics in atopic dermatitis that published on 2003 until 2018 for critical apprisal. From the review we concluded that probiotics can be considered for use as a therapy for the treatment of atopic dermatitis associated with food allergies.

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1. Introduction

Allergies are health problems that are frequently occurring in this decade. Zeiger on 2003 wrote that 4-6 % of children in United States were found to have food allergies[1]. According to a study on 2011, there were 38,480 children in the United States of less than 18 years of age that were found to have allergies to certain foods[2]. Approximately 6% of young children in the United States had a food allergy[3]. Atopic dermatitis (AD) is one of the clinical manifestations of food allergies. On the people with food allergies, atopic dermatitis appears as body reactions by the existence of allergens. Food allergies are related to the immune system[4]. When there was an interference on the immune system, then body reacted in the form of atopic dermatitis[5].

The presence of commensal bacterias in the intestinal immune system specify the body reaction on food allergens. The alteration of commensal bacterias composition in the intestinal immune system triggers series of useful pathological reactions, and the disadvantageous one as well. Probiotics are living microorganism colonize in the intestine.The presence of probiotics in the intestine can alter the commensal bacterias composition, so that affect the intestinal immune system. There were several researches reported the advantages of probiotics on some health problems, especially those associated with immune system. This matter associated with probiotics capability as immune regulators on intestinal immune system, making it as an alternative solution (or therapy?) for atopic dermatitis[6].

2. Discussion

Atopic dermatitis

The skin ailment atopic dermatitis (AD) is also called eczema[7]. AD is an ailment with various causes and is affected by genetics[8]. AD is a chronic skin ailment that can affect the health of a person, and for this reason, therapy and management of AD continues to be developed. AD is a condition of chronic skin inflammation that are marked by pruritus,lesions and dry scaly skin. Acute lesions in AD are marked by papula pruritus with erythema, excoriation, and serous exudate[9]. Chronic AD is marked by areas of lichenification and fibrotic nodules, often accompanied by acute lesions. AD is a health problem that commonly occurs among children. In developing countries, the prevalence of AD is 20 % [10]. The cause of one-third of AD sufferers of moderate to severe levels is food allergies[11].

Food allergy

Food allergy is a pathological reaction toward certain proteins that is mediated by a chain of immunological reactions. Food allergy is a health problem that involves specific immune responses when a sufferer is exposed to allergens in the form of certain food proteins. Many food ingredients have allergenic effects. Milk and dairy products, peanuts, eggs, soybeans, wheat, seafood, and shellfish are several foods that may cause allergies[12].

The immune system is the defense system of the body, which may pathologically respond to allergens through the phases of sensitization and elicitation. The sensitization phase involves T cells and T helper-2 (Th-2) cells, where the response that occurs is related to the production of interleukins IL-4, IL-5, and IL-13 from T-CD4 cells. In the sensitization phase, Th-2 will stimulate the production of immunoglobulin E (IgE) when the body is exposed to allergens. IgE then occupies the receptor on the mast cell surface. The elicitation phase occurs several moments after the body is exposed to allergens. In this phase, the IgE complex bound to the receptor on the mast cell surface will become active when the body is exposed to the same allergen, which leads the body to respond to the allergen[13].

In AD, there are abnormalities in the cutaneous immune system and systemic immunity marked by the increase in IgE serum, increase in FcεRI in Langerhans cells and epidermal dendritic inflammation cells, and the increase in T cells related to the lymphocyte receptors on the skin[14]. T cells in AD do not only cause an increase in Th2 cytokines but also cause the production of heterogeneous cytokines that involve interferon (IFN) γ and interleukin (IL) 17 [15]. This increase in cytokines is what will activate the body to respond in the form of inflammation.

Intestinal immune system

The intestines, part of the digestive tract, is the largest immune system in the human body. Most of the production of antibodies that fight allergens in the human body occur in the intestines. This is affected by the composition of microbes that can stimulate the immune system.

In countering allergies caused by allergens, microbes in the digestive tract have a role in the induction, training, and function of the immune system,including regulation of T cells and Th17 cells[16]. Commensal microbes in the intestines have several benefits. The function of commensal microbes included the production of nutrients, detoxification, protection against pathogens, and regulation of the immune system. The contribution of intestinal microbes in countering allergies is by modulating innate lymphoid cells and acting directly on T regulator cells through toll-like receptors (TLRs) [17, 18].

Bacteroides and *Clostridia* colonize colonize in the intestine. Bacteroides microbes are gram negatives, colonize in the intestine[19]. The *Bacteroides* affects the intestinal epithelial, the cells which possess some benefits by inducing cytokines production that will interact with lymphocytes. *Bacteroides thetaiotaomicron* is one of the *Bacteroides* genus, which able to induce the production of RegIIIγ, an antimicrobial peptide, through the specialized IECs (intestinal epithelial cells) known as paneth cell[20]. *Bacteroides fragilis*, another member in the genus, affects the increasing production of T helper (Th1) cell. Other than that, *B. fragilis* also affects the mucosal T cell homeostatic and regulation[21].

Clostridia are Gram-positive microbe consist of several clusters based on genomic similarity[22]. *Clostridia* XIVa and IV are are not human toxigenic. *Clostridia* XIVa consists of genera *Clostridium*, *Coprococcus, Eubacterium*, *Roseburia and also Ruminococcus*. Meanwhile cluster IV

group includes species belonging to the *Clostridium*, *Faecalibacterium* and *Ruminococcus* genera[23]. The lowering level of *Clostridia* XIVa and IV in the intestine is associated with atopy in the childhood[24]. *Clostridia* induces T cell regulator (T reg) activity, then stimulates IL 10 to suppress the disadvantageous effects of Th 17 cells[25].

Intestinal microbes in the digestive tract are the largest antigen components in the human body. The composition of microbes in the intestines affect the epithelial membrane and the immune system in the intestines, and thus microbes can affect the health of humans. Intestinal microbes in the digestive tract affectsthe pathogenesis of AD in relation to the immune system[26].

Probiotics as immune system regulators

Probiotics are living microbes that form colonies in the intestines[27]. According to the WHO, probiotics are defined as living microorganisms that can improve the health of humans when given in the proper amounts[28]. Another definition states that probiotics are living organisms with or without low pathogenic effects that may be beneficial to human health[29].

Probiotics affect the immune system because they may regulate the function of systemic and mucosal immune cells, and also affect intestinal epithelial cells[30]. Probiotics can increase the response of nonspecific cellular immunity, marked by the activation of natural killer (NK) cells and macrophages[31]. Probiotics affect the differentiation of T lymphocytes,which are specific antigens, and the release of various cytokines[32]. Probiotics can also change the composition of intestinal microbes and affect the production of cytokines. Probiotics can also modulate receptors that resemble toll receptors and proteoglycan proteins from enterocytes, triggering the activation of dendritic cells and Th1 response. Stimulation of Th1 cytokines can suppress the effectfrom Th2, which modulates allergic reactions. In addition, probiotics stimulate the increase in mucosal IgA[33].

Lactobacillus and *Bifidobacterium* strains are general used probiotics and widely acknowledged health-promoting and immunomodulatory properties[34]. *Lactobacillus* provides immune system regulation effect by increasing the level of IL 10, IL 12, and cytokine[35]. *Lactobacillus rhamnosus, member of Lactobacillusstrain,* possess the ability of inhibiting the activity of tumor necrosis factor (TNF), IL-6, keratinocyte chemoattractant, and interferon (IFN)-γ, making this microbe play a role in regulation of innate immunity and the Th1 immune response[36].

A double-blind, placebo-controlled study had been done to evaluate the probiotic effect of *Lactobacillius strain* on the immune system. The study reported that *L. acidophilus* regulated genes mediating immune response, hormonal regulation of tissue growth and development, and ion homeostasis. Meanwhile *L. casei* affects Th1–Th2 balance with upregulation of IL-17D and IL-21, which enhance the development of natural killer cells[37].

Bifidobacterium is a probiotic that able to maintain the intestine and effect on human health by the mechanism of immunomodulation of both mucosal and systemic immunity under healthy or pathogenic conditions. *Bifidobacterium* can stimulate immune cells to produce different cytokines that direct the polarization of naïve $CD4^+$ T cells towards different effector or regulatory T cell subsets[38].

Effects of probiotics on atopic dermatitis

Probiotics have a positive effect for allergy therapy. The presence of probiotics in intestinal microbial components correlates with the ability of the body in countering allergies, including atopy. Several studies have been conducted to research the effects of probiotic treatment on the occurrences of atopic dermatitis caused by food allergies.

In a double-blind, placebo-controlled, crossover study, testing was carried outfor the effects of treatment of lyophilized *Lactobacillus rhamnosus* 19070-2 and *Lactobacillus reuteri* DSM 122460 on children for a period of 6 weeks. Testing results indicated that 56% of the children experienced recovery from their eczema conditions. This was apparent for AD sufferers who had allergies with a p value = 0.02 [39].

From a meta-analysis of 25 randomized controlled trials that involved children from 1 to 18 years of age, there was an indication of reduced values of Scoring Atopic Dermatitis (SCORAD) with treatment of probiotics (-5.74, 95% confidence interval -7.27 to -4.20). The research found that probiotics can be used as an alternative treatment for atopic dermatitis[40].Other study was conducted to test the effects of probiotics on children who suffered from AD. Study results found that the average SCORAD score for the group who received probiotics was 26.0 (21.9-30.8) while for the placebo group it was 35.1 (28.9-42.8) with a p value = 0.02. For children who were sensitive toward food, the average SCORAD value was 0.73 (95% CI 0.54-1.00, P=0.047). From these results, it was found that probiotics can provide an effect of recovery for children from AD conditions[41].

3. CONCLUSION

In relation to the immune system, probiotics can regulate the immune system to provide a response to the presence of allergens. Probiotics may be considered to be used as therapy for the treatment of atopic dermatitis related to food allergies. However, further studies need to be conducted to clarify the potential effects of probiotics on atopic dermatitis caused by food allergies.

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