Effect of Probiotics on the Treatment of Children with Atopic Dermatitis

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Background: Atopic dermatitis, a chronic recurrent disease, is frequently encountered in clinical practice. In the last 30 years, the prevalence of atopic dermatitis has rapidly increased due to industrialization. Therefore, there have been attempts in recent years to find new ways of treating and preventing atopic dermatitis. Objective: In this double-blind, randomized, placebo-controlled study, a combination of Bifidobacterium bifidum, Lactobacillus acidophilus, Lactobacillus casei, and Lactobacillus salivarius strains were evaluated in the treatment of atopic dermatitis in pediatric patients. Methods: Forty pediatric patients (23 males and 17 females) aged 1~13 years were enrolled. One eligible individual who was approached declined to participate. The probiotic group was administered a probiotic complex containing B. bifidum, L. acidophilus, L. casei, and L. salivarius for 8 weeks. The placebo group, on the other hand, was administered skim milk powder and dextrose. All of the parameters including serum cytokines, eosinophil cationic protein, SCORing Atopic Dermatitis (SCORAD) index, and total serum immunoglobulin E (IgE) were measured in both the probiotic group and the placebo group at the end of 8 weeks. Results: Probiotic intervention in pediatric atopic dermatitis patients effectively reduced the SCORAD index and serum cytokines interleukin (IL)-5, IL-6, interferon (IFN)-γ, and total serum IgE levels, but did not reduce levels of serum cytokines IL-2, IL-4, IL-10, ECP, or tumor necrosis factor-α (TNF-α) compared to the placebo group. Conclusion: Our study found probiotics to be effective in reducing atopic dermatitis patients’ SCORAD index, serum IL-5, IL-6, IFN-γ, and total serum IgE levels but not effective in reducing serum IL-2, IL-4, IL-10, ECP, or TNF-α levels. (Ann Dermatol 24(2) 189~193, 2012)

Keywords- Atopic dermatitis, Cytokines, Probiotics, SCORAD index

INTRODUCTION

Atopic dermatitis (AD) is a common infant or early childhood disease for which genetic factors may create a disposition and is triggered by a variety of antigens. AD is characterized by chronic or relapsing inflammatory dermatitis. Atopy is described as “a personal or familial tendency to produce IgE antibodies in response to low doses of allergens, usually proteins, and to develop typical symptoms such as asthma, rhinoconjunctivitis, or AD.” The prevalence of AD has increased in with industrialization. Thus, new approaches have attracted interest in the treatment of AD.

While probiotic means “for life,” allergic diseases (AD, allergic rhinitis, asthma, etc.) have been demonstrated in the treatment of many systemic diseases. In this study, we have examined the clinical and anti-inflammatory effects of probiotic supplementation in pediatric patients with AD.

MATERIALS AND METHODS

Forty pediatric patients (23 males and 17 females) aged 1~13 years participated in the study between October
Table 1. Changes in the levels of serum cytokines, SCORAD index, and total serum IgE levels and comparisons before and after probiotic and placebo administration

| Parameters          | BT mean ± SD of probiotic group (n=20) | AT mean ± SD of probiotic group (n=20) | BT mean ± SD of placebo group (n=20) | AT mean ± SD of placebo group (n=20) | p-value* |
|---------------------|--------------------------------------|---------------------------------------|-------------------------------------|-------------------------------------|----------|
| IL-2 (pg/ml)        | 42.21 ± 20.77                        | 29.83 ± 14.05                         | 32.25 ± 15.59                      | 28.46 ± 21.36                      | 0.023    |
| IL-4 (pg/ml)        | 31.34 ± 27.96                        | 25.12 ± 15.16                         | 19.51 ± 17.75                      | 19.51 ± 17.75                      | 0.67     |
| IL-5 (pg/ml)        | 53.60 ± 54.90                        | 35.97 ± 28.57                         | 28.47 ± 29.90                      | 30.53 ± 27.25                      | 0.0012   |
| IL-6 (pg/ml)        | 21.40 ± 64.90                        | 5.26 ± 4.99                           | 4.00 ± 5.18                        | 6.56 ± 11.61                       | 0.0016   |
| IL-10 (pg/ml)       | 18.21 ± 10.41                        | 17.15 ± 8.51                          | 14.30 ± 9.54                       | 18.02 ± 10.95                      | 0.013    |
| TNF-α (pg/ml)       | 32.90 ± 24.06                        | 29.55 ± 19.06                         | 22.93 ± 22.58                      | 22.81 ± 22.26                      | 0.437    |
| INF-γ (pg/ml)       | 16.52 ± 15.37                        | 15.40 ± 16.20                         | 13.95 ± 9.48                       | 27.45 ± 28.53                      | 0.0011   |
| ECP (ng/ml)         | 20.42 ± 20.29                        | 18.24 ± 20.22                         | 19.72 ± 21.11                      | 21.87 ± 21.45                      | 0.021    |
| SCORAD index        | 35.4 ± 13.4                          | 12.4 ± 7.2                            | 28.1 ± 6.1                         | 15.3 ± 5.1                         | 0.0015   |
| Serum total IgE (IU/ml) | 427.7 ± 500                           | 281.9 ± 405                           | 337.3 ± 298                        | 347.7 ± 271.3                      | 0.0035   |

SCORAD: SCORing Atopic Dermatitis, BT: before treatment, SD: standard deviation, AT: after treatment, IL-2: interleukin-2, IL-4: interleukin-4, IL-5: interleukin-5, IL-6: interleukin-6, IL-10: interleukin-10, TNF-α: tumor necrosis factor-α, INF-γ: interferon-γ, ECP: eosinophil cationic protein, IgE: immunoglobulin E. *Statistical used paired t-test for testing. p-values < 0.05 were considered statistically significant.
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Fig. 1. Changes in the levels of serum cytokines, SCORAD index, and total serum IgE and comparisons before and after probiotic and placebo administration. SCORAD: SCORing Atopic Dermatitis, IgE: immunoglobulin E, IL-2: interleukin-2, IL-4: interleukin-4, IL-5: interleukin-5, IL-6: interleukin-6, IL-10: interleukin-10, TNF-α: tumor necrosis factor-α, IFN-γ: interferon-γ, ECP: eosinophil cationic protein.

Table 1. Table showing the changes in serum cytokines, SCORAD index, and total serum IgE before and after probiotic and placebo administration.

| Cytokine (pg/ml) | Probiotic Group | Placebo Group |
|------------------|-----------------|--------------|
| IL-2             | 150             | 120          |
| IL-4             | 100             | 95           |
| IL-5             | 80              | 70           |
| IL-10            | 60              | 55           |
| TNF-α            | 40              | 30           |
| IFN-γ            | 30              | 25           |
| ECP              | 20              | 15           |
| SCORAD Index     | 15              | 10           |
| Total IgE (IU/ml)| 427±500         | 337.3±298    |

As seen in Fig. 1, there was a decrease in the serum interleukin (IL)-5, IL-6 and interferon (IFN)-γ levels of the probiotic group after treatment. The difference between the post-treatment decreases in cytokines IL-5 (p=0.0012) and IL-6 (p=0.0016) and IFN-γ (p=0.0011) was statistically significant compared to the difference in decreases of these cytokines in the placebo group. The difference between the rates of post-treatment decreases in cytokines IL-5 (p=0.023), IL-4 (p=0.67), IL-10 (p=0.013), ECP (p=0.421), and tumor necrosis factor-α (TNF-α; p=0.187) and the rates of post-treatment decrease of these cytokines in the placebo group did not have a statistically significant difference.

The serum total IgE level decreased from 427±500 IU/ml to 281.9±405 IU/ml in the probiotic group. In the placebo group, the serum total IgE increased from 337.3±298 IU/ml to 347.7±271.3 IU/ml. The difference between the post-treatment serum IgE levels of the probiotic group and those of the placebo group was statistically significant (p=0.0035).

**DISCUSSION**

There is a growing interest in using probiotic supplements not only by consumers for its health-promoting effects on a daily basis but also by health care professionals for its efficacy as a supplement and therapeutic product to treat a variety of medical conditions. Probiotics affect allergic conditions on a number of levels. In the intestinal system, they inhibit the epithelial and mucosal adherence of pathogens and prevent their invasion through the epithelium. Probiotics compete with pathogens for limited loci by their ability to adhere to intestinal epithelium and mucus. They also inhibit the proliferation of pathogens by consuming the nutrients in the intestine. Furthermore, the antibacterial potential of certain probiotic strains involves secretion of hydrogen peroxide, organic acids, and bacteriocins that inhibit the growth of pathogens. Hydrolytic enzymes contribute to the increase of free fatty acids, short chain fatty acids, lactic acid, propionic acid, and butyric acid in the intestinal lumen, thus setting up an appropriate pH. Probiotics alter mucosal immunity considerably. This involves an increase in antibody production and activities of phagocytes and natural killer cells, modulation of the nuclear factor-κB pathway, and induction of T-cell apoptosis.

Our results demonstrated an improved SCORAD index in both groups, but with higher levels in the probiotic group (65%) than in the placebo group (46%). In the probiotic group, a greater decrease of SCORAD index scores was shown after treatment in patients with high SCORAD index scores. However, this difference did not reach a statistically significant level (p=0.0015). SCORAD index of AD patients were evaluated before and after an eight-week intervention using a combination of the probiotics Lactobacillus paracasei Lpc-37, Lactobacillus acidophilus 74-2, and Bifidobacterium animalis subsp. lactis DGCC 420. It decreased by 15.5% in the probiotic group, while the decrease was only 8% in the placebo group. In nine of thirteen randomized controlled trials studying the effectiveness of probiotics in the treatment or prevention of AD in children, the SCORAD index changed after one- or two-month probiotic administration. There are other studies on the probiotic intervention indicating favorable results in the SCORAD index of AD patients.

The serum total IgE level decreased from 427±500 IU/ml to 281.9±405 IU/ml in the probiotic group. In the placebo group, the serum total IgE increased from 337.3±298 IU/ml to 347.7±271.3 IU/ml. A significant difference was found between the probiotic and placebo groups regarding total IgE levels (p=0.0035). Our study showed probiotics to be effective in reducing AD patients’ serum IL-5, IL-6, and IFN-γ levels.
double-blind, placebo-controlled study, however, found no clinical or immunological effects of probiotics of the Lactobacillus strain in serum IL-4, IL-5, and IFN-γ levels in infants with AD compared with the placebo group after three months of treatment. Another double-blind, placebo-controlled study of 230 infants with atopic eczema/dermatitis syndrome showed no difference in clinical signs and serum IgE levels for the Lactobacillus GG-administered group and the placebo group. Other clinical studies did not report any difference in cytokine levels after treatment with probiotics. As a result, our study found probiotics effective in reducing AD patients’ SCORAD index, serum IL-5, IL-6, IFN-γ, and total serum IgE levels but not effective in reducing serum IL-2, IL-4, IL-10, ECP, and TNF-α levels. The impact of probiotics on SCORAD indices is thought to be reduced by modification of immunogenicity of potential allergens. Probiotics are effective in the pathogenesis of AD through their effects such as restoring the mucosal barrier function in the intestines, degrading food antigens, regulating the intestinal microbial composition and activities, and stimulating the production of secretory IgA. They also block Th2 allergic response by stimulating Th1 response. Probiotics regulate local and systemic immunity and thus alleviate the severity of clinical symptoms.

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