

The Effects of Probiotic *Lactobacillus casei* in Allergic Rhinitis Patients

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ABSTRACT

Allergic rhinitis is inflammatory reactions mediated by immunoglobulin E, after exposure to allergens. Allergic rhinitis can be alleviated by the use of specific probiotics to confer immune effects. The specific strains used in this study were selected based on their anti-inflammatory properties and an expected in promoting a Th1 type of immune response. To review the benefits of probiotics of *Lactobacillus casei* in preventing allergy attacks which inhibit the production of IgE, IL-4 and in reducing the symptoms. The study design was quasi-experimental with pre and post test design. The subjects were 45 patients who had a history of allergic rhinitis and filled out the questionnaires to get the allergic symptoms. The blood samples were taken for examining the IgE and IL-4 levels then after giving milk containing probiotics for 1 month, the researcher did the same examination. The mean IgE and IL-4 levels decreased before and after probiotics supplementation from 291.88 IU /L and 22.48 pg/ml to 141.43 IU/L and 17.83 pg/ml. The result of the statistical analysis paired t-test test was $p = 0.00$ on IgE level and $p=0,056$ on IL-4 level. The allergic rhinitis symptoms decreased significantly, the patients who had persistent symptom reduced from 28 patients to 2 patients. Based on the Wilcoxon signed rank test showed a significance value of $P = 0.00$. Probiotics is useful in preventing allergy attacks that inhibit the production of IgE, IL-4 and reduces the symptoms.

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1. INTRODUCTION

Allergic rhinitis is defined clinically by the symptoms caused by immunologically mediated (mostly IgE-dependent) inflammation after the exposure of the nasal mucous membranes to offending allergens. Symptoms of allergic rhinitis including rhinorrhea, nasal obstruction or blockage, nasal itching, sneezing, and postnasal drip reverse spontaneously or after treatment. Allergic rhinitis is a common chronic inflammatory disorder with an increasing trend of prevalence worldwide over the last few decades become a global health problem, affecting approximately 10 to 25% of the population [1]. Many of treatment modalities are employed to control the symptoms but there is no cure because they do not act through modification of inflammatory pathways which underlies the pathophysiologic basic of the disease [2]. Recently, in vitro experiments suggest that lactic acid bacteria (LAB) can inhibit Th2 cytokine production by mononuclear cells from patients with allergies [3]. Moreover, a landmark article demonstrated that LAB was effective in preventing early atopic disease in high-risk children [4]. With these encouraging reports, the efficacy of probiotics for the management of allergic disease has begun to be highly appreciated. We sought to ascertain whether the immunologic benefits of probiotics could translate into clinical improvement. The current

understanding suggests that the probiotic organisms reverse increased intestinal permeability, enhance gut-specific IgA responses, promote gut barrier function through restoration of normal microbes, and enhance transforming growth factor beta and interleukin-10 production as well as cytokines that promote production of IgE antibodies [5],[6]. The role of T-helper 1 (Th1) enhancement and T-helper 2 (Th2) reduction remains to be proven. Probiotics are perceived to exert beneficial effects in the prevention and treatment of allergic diseases via modifying the gut ecosystem.

The aim of this study was to assess whether ingestion of fermented milk containing *Lactobacillus casei* L Shirota strain can improve the quality of life of the patients with allergic rhinitis symptoms and reduce on blood immunologic parameters allergic (IgE, IL-4).

2. RESEARCH METHOD

The study was performed from January 2013 through March 2013. The patients were recruited from the students of Faculty of Medicine and Health Science, Muhammadiyah University of Yogyakarta, Indonesia. The study design was quasi-experimental with pre and post test design. The subjects were 40 students; the diagnosis of allergic rhinitis was made according to a history of allergic rhinitis and positive skin prick test result and filled out the questionnaires to get the allergic symptoms. Before and after probiotic supplementation, a blood sample for analysis of IgE in serum (sIgE) and IL-4 was drawn, Serum IgE and IL-4 was analyzed by using ELISA. The normal reference interval sIgE level was 0 to 100 kIU/L and IL-4 level was 0-65 pg/ml.

3. RESULTS AND ANALYSIS

Initially, 45 students who were included in the study filled out the questionnaires to get the allergic symptoms and blood sample for IgE in serum (sIgE) and IL-4 analysis. There were five students who did not participate for the second blood sample because they were sick. Thus, the distribution of characteristic respondents and their clinical characteristics degree of symptoms are shown on Table 1.

Table 1. Characteristics of Respondents

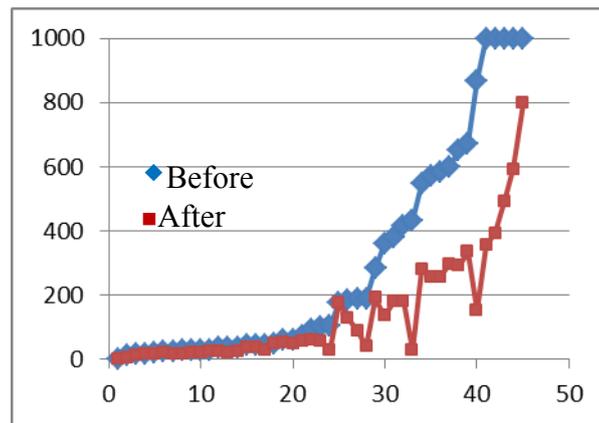
Variable		Number	Percentage (%)
Gender	Male	11	27.50
	Female	29	72.50
Atopic	Yes	31	77.50
	No	9	22.50
Family	Yes	20	50.00
	No	20	50.00
IL-4	Normal	36	90.00
	Increase	4	10.00
Ig E	Normal	18	45.00
	Increase	22	55.00
Symptoms	<i>mild intermittent</i>	11	24.44
	<i>moderate intermittent</i>	6	13.33
	<i>severe intermittent</i>	0	00.00
	<i>mild persistent/moderate persistent</i>	20	44.44
	<i>severe persistent</i>	8	17.78

Sources: Primary data

The average IgE levels before the intervention was 291.88IU/L, and after probiotics supplementation was 141.43IU/L. The reduction of IgE level after the probiotic supplementation is shown on Figure 1. This result is different from another study which stated that the effects of probiotics to modulate blood/immunologic parameters are associated with allergic symptoms. In some studies, the beneficial effects on clinical parameters are found without significant change in the immunologic parameters.

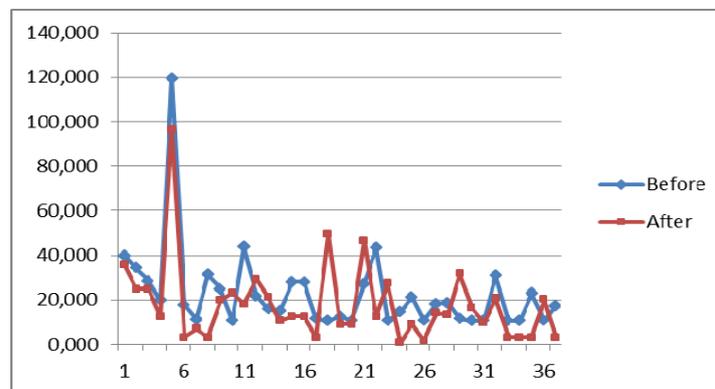
The average IL-4 level before the probiotic supplementation was 291.88IU/L and after the probiotic supplementation was 141.43IU/L. The reduction of IL-4 level after the probiotic supplementation is shown on Figure 2.

This phenomenon shows the causal relationships between microbes and allergy challenges and helps to define the limits of T H1/TH2 relevance to these diseases. The original paradigm of a reciprocal relationship between TH1 and T H2 might only be relevant to immune development before the establishment of these diseases. This is consistent with numerous studies which documenting the increase of T H1 and TH2 cells in allergic airways. Intestinal microflora can contribute to the process of food antigens in the gut and probiotics could modify the structure of potential antigens and reduce their immunogenicity [7].



Sources: Primary data

Figure 1. Serum IgE test results before and after the probiotic supplementation



Sources: Primary data

Figure 2. Serum IL-4 test results before and after the probiotic supplementation

The clinical manifestations of allergic rhinitis before the probiotics supplementation were classified as follows: persistent moderate was (17.78%), the persistent mild (44.44%), the intermittent moderate was (13.33%), and the intermittent mild was (24.44%). Meanwhile after the probiotic supplementation, the results were classified as follows: the persistent moderate was (0%), the persistent mild (4.44%), the intermittent moderate (2.22%), and the intermittent mild (93.33%). After being tested with the Wilcoxon signed rank test, the result showed a significance value of $P=0.00$ as shown on Table 2.

Table 2. The effect of probiotic supplementation to clinical manifestation allergic rhinitis (in percentage)

	Intermiten			Persisten			p
	Mild	Moderate	Severe	Mild	Moderate	Severe	
Before	24.44	13.33	0	44.44	17.78	0	0.00
After	93.33	2.22	0	04.44	0	0	

3.1. Discussion

Probiotics have been used to reduce the risk allergy such as atopic eczema, frequently the first allergic symptom to manifest itself in children. Previous intervention studies showing risk reduction for eczema have failed to reduce the risk of another allergic disease likes respiratory allergies. This may be due to strain and host specific characteristics [8]. In fact, in vitro studies using human mononuclear cells have indicated that there are strain-dependent differences in the ability of lactic acid bacteria to induce

immunoregulatory monokines such as interleukin. Contribution of the species and strain-specific nature of lactic acid bacteria on the efficacy of improving allergic symptoms should be considered [9].

In this study, we found a significant overall change in immunologic parameters in the probiotics group. The average IgE levels before the supplementation was 291.88 IU/L, and after the supplementation was 141.43 IU/L and the average IL-4 levels before the supplementation was 291.88 IU/L, and after the supplementation was 141.43 IU/L. The result of the statistical analysis paired t-test test was $p = 0.00$ on IgE level and $p = 0.056$ on IL-4 level.

The process of allergic responses in the nasal cavity is allergen sensitization that antigen presenting cells (APCs) engulf allergens upon the encounter. The allergens are then broken down into peptide segments, which are later presented to native T cells (Th0 cells) once the APCs migrate into the lymph nodes. This interaction between APCs and Th0 cells leads to the multiplication and differentiation of Th0 cells, giving rise to either Th1 or Th2 cells. Th2 cells have the ability to bind with B cells, triggering their transformation into plasma cells that can produce and secrete IgE into blood circulation. The significant reduction of IgE level after probiotics supplementation in this study showed that the effects of probiotics to modulate blood/immunologic allergic parameter, contrary to previous studies that report no statistical difference was found at baseline or at 12 months of probiotics intervention between intervention and control groups for any examined immunologic parameter [10].

Th1 cells were identified with CD4+, IFN- γ +, and IL-4-, while Th2 cells were identified with CD4+, IFN- γ -, and IL-4+. The cytokine profile of Th2 cells is pro allergenic, primarily because IL-4 promotes the class switching of immunoglobulins in B cells, giving rise to the synthesis of allergen-specific IgE [8] the study report the decreasing of IL-4 level after supplementation probiotic but no statistical significant. Similar to previous studies [11],[12] probiotic therapy was accompanied by only moderate changes in production of the cytokines IL-4, IFN- γ , IL-10, and IL-2. IL-4 stimulates B lymphocytes to produce IgE. Moreover, it is possible that a longer period of treatment might be required to produce significant decreases in IL-4 levels [13].

In the systematic review [2], treatment with probiotic was shown to improve the quality of life score of patients with allergic rhinitis at the end of treatment. Other studies showing improvement with probiotic treatment decrease in the number of episodes of rhinitis per year. Pooling could not be undertaken for many of the outcomes, as studies did not follow a standard format for reporting of clinical trials. Many reasons could account for the different outcomes among studies wherever pooling was done in these trials and these are: varied dose and intake period, the type and severity of the symptoms involved were different, seasonal variation of allergic symptoms and most importantly, the species and strains of the probiotics differ.

In this study the outcome measures were the time (number of days) of allergic symptom present at one week and the symptom disturb daily activity or not (ARIA classification).

4. CONCLUSION

In summary, the probiotics supplementation of *Lactobacillus casei* LShirota strain to students with allergic rhinitis symptom was associated with a moderate improvement in the clinical severity of symptom. In suggesting a more pronounced effect in allergic patients, our results are in accordance with results from experimental studies, as well as those of previous clinical trials. Future studies should address the effects of long term probiotic supplementation.

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