

Probiotic therapy on children with allergic rhinitis

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Abstract

Background Inflammation of the mucosal epithelium by eosinophils in nasal secretions of patients with allergic rhinitis may cause persistent nasal blockage. A common therapy for allergic rhinitis is oral or intranasal corticosteroids. However, corticosteroids carry the risk of disrupting growth and development in children. Probiotic treatment in allergic rhinitis patients works by manipulating the bacterial ecosystem of the digestive tract, stimulating the balance of Th1 and Th2 immune responses.

Objective To assess the effects of probiotic supplementation on eosinophil levels in nasal secretions, duration of allergic episodes, and total nasal symptom scores in children aged 2-18 years with allergic rhinitis.

Methods A randomized, double-blind, controlled trial was performed on children aged 2 to 18 years who visited Sanglah Hospital, Denpasar, between March to July 2012 due to allergic rhinitis. Fifty-five eligible subjects were involved in the study. Subjects were randomly allocated to receive either standard therapy (antihistamines) and probiotics or standard therapy and placebo for 30 days. Mann-Whitney test was used for statistical non-parametric unpaired samples analysis. P values of <0.05 were considered to be statistically significant.

Results Fifty-five subjects with allergic rhinitis were randomized into either the probiotic group (27 subjects) or the placebo group (28 subjects). We found that the median (range) nasal eosinophil percentage reduction before the study compared to after 30 days of treatment was higher in the probiotic group than in the placebo group (34 (15-65) vs 6 (0-24) %, respectively, $P < 0.0001$). Median (range) duration of allergic rhinitis episode in the probiotic group was shorter compared to the placebo group (48 (0-96) hours vs 72 (6-168) hours, respectively; $P < 0.0001$). The median (range) total nasal symptom score was also lower in the probiotic group compared to the placebo group (2 (0-3) vs 5 (1-6), respectively; $P < 0.0001$).

Conclusion Probiotic supplementation reduces the percentage of nasal eosinophils, duration of allergic rhinitis episode, and total nasal symptoms. [Paediatr Indones. 2013;53:264-7.].

Keywords: allergic rhinitis, children, probiotic

Allergic rhinitis is an inflammation in the nose characterized by nasal symptoms with anterior or posterior rhinorrhea, sneezing, nasal obstruction, or itching.¹ Prevalence of allergic rhinitis have been reported to be 10-20% in North America, 10-15% in Europe, about 20% in Thailand, 10% in Japan, and 10-26% of all ear-nose-throat (ENT) patients in a few large hospitals in Indonesia.² Patients with allergic rhinitis usually have persistent nasal obstruction, due to high eosinophil levels in nasal secretions that lead to stimulation of the nasal mucosal epithelium. Allergic rhinitis is considered to be present when nasal secretion examinations reveal eosinophils of >3%.³ One therapeutic modality for allergic rhinitis is corticosteroids. Corticosteroids are excellent in reducing inflammation in allergic rhinitis, but in children they have a potential risk of disturbing growth and development.

Probiotics are living, microbial supplements that improve the intestinal microfloral balance in humans.⁴ Probiotics have a unique role on allergic disease prevention and treatment. Probiotics stimulate T regulator that inhibit Th2 reactivity and excessive Th1 activity.⁵

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There have been few studies on the role of probiotics in allergic rhinitis treatment, particularly on nasal eosinophil cells, although several have reported that probiotics have a curative effect on allergic diseases.⁶⁻⁸ To date, studies on the relationship of probiotics and allergic rhinitis and allergic rhinitis symptoms that persist throughout years have been limited. Based on these considerations, we aimed to assess the effects of probiotics in children with allergic rhinitis on reducing the nasal eosinophil percentages in nasal secretions, duration of allergic episodes, and total nasal symptom scores.

Methods

A randomized, double-blind, controlled trial was undertaken on children 2 to 18 years of age with allergic rhinitis symptoms who visited Sanglah Hospital, Denpasar, between March 1 to July 15, 2012. Eligible patients were chosen by consecutive sampling. This study was approved by the Research Ethics Committee of Udayana Medical School, Sanglah Hospital, Denpasar.

The inclusion criteria were patients with allergic rhinitis, aged 2 to 18 years, whose parents agreed to participate in this study. We excluded those with a history of cigarette smoke exposure in the 6 months prior to the study or those who were using corticosteroids. The minimum sample requirement was measured using $P=0.05$, power 90%, and calculated to be 27 in each group.

Fifty-five eligible subjects were randomized into two groups (probiotic or placebo). One group received standard therapy with probiotics (probiotic group), while the other group received standard therapy with placebo (placebo group). Randomization was done with 6-block randomization table and concealed until the end of study. We performed intra-observer agreement for the laboratory officers before the study. We measured nasal eosinophil percentages in nasal secretions from subjects at day 0 and 30.

The probiotics used in this study contained *Lactobacillus acidophilus*, *Bacillus clausii*, *Lactobacillus paracasei*, *Lactobacillus casei*, and *Lactobacillus rhamnosus* species at 10^{11} CFU/sachet and administered once daily for 30 days. Probiotics and placebo were packaged similarly and coded by the pharmacy personnel.

After the study was complete, the list of probiotic and placebo codes was given to the researcher.

Nasal swab eosinophils before and after treatment (probiotics or placebo) was taken after history-taking and physical examination. Skin prick test was conducted to establish the allergic rhinitis diagnosis. Skin prick test was performed by the researcher and examination of nasal swab eosinophils was done by the recruited laboratory officer. Standard therapy for allergic rhinitis in this study was oral, second-generation antihistamine (cetirizine) at a dose of 0.25 mg/kg body weight once daily. Adherence, tolerance, and side effects of the treatment for both treatment groups were monitored by phone on the 7th, 14th, 21st, and 30th days.

For nasal symptom scores, the patients rated sneezing, rhinorrhea and nasal congestion as either absent, slight, moderate or severe, corresponding to the numerical values 0, 1, 2, and 3, respectively. By adding the score for each of the three symptoms, a sum of between 0 and 9 was obtained.

Durations of allergic rhinitis episodes was measured with the duration in hours on when allergic rhinitis symptom was appear to the time when the symptom resolved.

We use SPSS version 16.0. Normality test was done if the data distribution was not normal, and data transformation was conducted. We present numerical data in median (interquartile range) for non-normal distribution and Mann-Whitney results for statistical, non-parametric, unpaired samples test analyses. The level of significance (α) was determined to be at $P<0.05$.

Results

During the study period there were 70 children admitted to Sanglah Hospital due to allergic rhinitis. Sixty-eight children met the inclusion criteria, eight children out of them were excluded due to their history of taking corticosteroids. Furthermore, we were unable to acquire a second nasal eosinophil examination from five other subjects. Hence, our study included 55 eligible subjects (**Figure 1**).

Subjects' characteristics are presented in **Table 1**. There were similar numbers of males and females in both groups. Median age (interquartile range) of the probiotic and placebo groups were 84.0 (24-147)

months and 79.5 (30-200) months, respectively. History of paternal atopy in the probiotic and placebo groups were 18/27 and 19/28, respectively. Asthma, as an allergy other than allergic rhinitis in the probiotic and placebo groups was noted in 16/27 and 18/28, respectively. Nine percent of children had mild allergic rhinitis and 91% had moderate allergic rhinitis.

Median percentage of nasal eosinophils at the beginning of treatment was not significantly different ($P=0.482$) between the probiotic and placebo groups. However, it was significantly different at the end of treatment. The median difference in the percentage reduction of nasal eosinophils, at the beginning of the study compared to the end of the study, was higher in the probiotic group than in the placebo group (34 (15-65) vs 6 (0-24) %, respectively; $P<0.0001$) (Table 2). Likewise, duration of allergic rhinitis episodes in the probiotic group was significantly shorter compared to that of the placebo group (48 (0-96) hours vs 72 (6-168) hours, respectively; $P<0.0001$). Total nasal symptom scores were also lower in the probiotic group compared to the placebo group (2 (0-3) vs 5 (1-6), respectively; $P<0.0001$) (Table 3).

Table 1. Characteristics of study subjects

Characteristics	Probiotic group (n=27)	Placebo group (n=28)
Gender, n		
Males	14	14
Median age (interquartile range), months	84.0(24-147)	79.5(30-203)
History of atopy, n		
Paternal	18	19
Maternal	7	8
Both parents	2	1
Another allergy, n		
Asthma	16	18
Dermatitis	3	6
Others	3	1
None	5	3

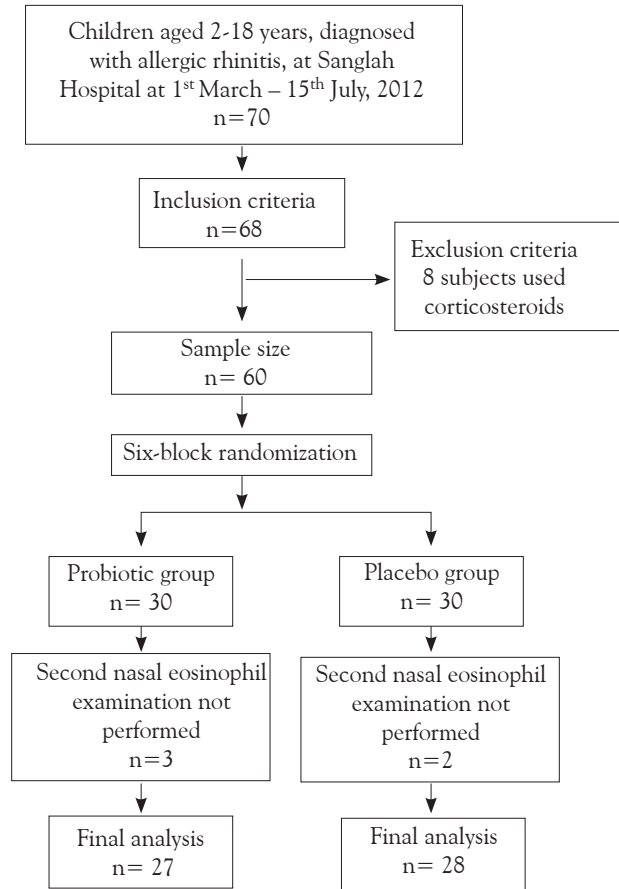


Figure 1. Study profile scheme

Discussion

The aim of this study was to assess probiotic effectiveness on nasal eosinophil levels in children with allergic rhinitis. Previous studies reported inconsistent results with probiotics usage, either as therapy or prevention, in children with allergic rhinitis. In this study, we found a statistically

Table 2. Comparison of nasal eosinophil levels in the probiotic and placebo groups

Percentage of nasal eosinophils	Probiotic group	Placebo group	P value
Median at the beginning of the study (interquartile range), %	34 (15-72)	35 (20-45)	0.482
Median at the end of the study (interquartile range), %	0 (0-25)	29 (16-41)	<0.0001
Median reduction (interquartile range), %	34 (15-65)	6 (0-24)	<0.0001

Table 3. Duration of illness episodes and total nasal symptom scores

Variables	Probiotic group	Placebo group	P value
Median duration of episode (interquartile range), hours	96 (0-168)	84 (24-168)	0.666
Median duration of episode with intervention (interquartile range), hours	48 (0-96)	72 (6-168)	<0.0001
Total nasal symptom score (TNSS)			
Median TNSS before (interquartile range)	6 (3-8)	6 (3-7)	0.694
Median TNSS after (interquartile range)	2 (0-3)	5 (1-6)	<0.0001

significant reduction of the percentage of nasal eosinophils in children with allergic rhinitis who were given probiotics plus standard therapy compared to those given placebo plus standard therapy ($P < 0.0001$). Similarly, an Italian study in which a 3-weeks probiotic supplementation therapy in children with allergic rhinitis showed a significant decrease of eosinophils in nasal smears with a 9% difference compared to the group with standard therapy plus placebo.⁶ A meta-analysis of probiotic supplementation consisting of different probiotic species (*Bifidobacterium longum*, *Lactobacillus acidophilus*, *Bacillus clausii*, *Lactobacillus paracasei*, *Lactobacillus casei*, and *Lactobacillus rhamnosus*) for 4 weeks as allergic rhinitis and asthma therapy, revealed that 9 out of 12 studies reported that probiotic supplementation provided beneficial effects in children with allergic rhinitis and significant improvements in symptoms compared to placebo.¹⁰

We gave 30 days of probiotics, consisting of different species including *Lactobacillus acidophilus*, *Lactobacillus casei*, *Bifidobacterium longum*, *Lactobacillus salvarius*, *Bifidobacterium infantis*, *Bifidobacterium lactis*, *Lactococcus lactis*, *Lactobacillus rhamnosus*, resulting in favorable outcomes for allergic rhinitis. We also found that episodes of illness were significantly shortened in the probiotic and standard therapy group compared to the placebo and standard therapy group. These results were consistent with a review that probiotics supplementation (*Lactobacillus acidophilus* and *Bifidobacterium*) for allergic rhinitis was shown to be an immune response enhancer and modulator, that may effectively and safely prevent and/or cure children with allergic rhinitis.¹¹

We also found that total nasal symptom score (TNSS) was significantly decreased in the probiotic group compared to the placebo group. Similarly, Ciprandi *et al.* reported that TNSS was significantly decreased in the probiotics group, with total scores of 7 ± 0.8 before treatment and 3.7 ± 0.7 after treatment.⁶

Our subjects reported no side effects of probiotics supplementation, similar to many reports on the lactobacillus strain, which has been used and proven to be safe for more than 70 years, and based on controlled clinical research showing that *Lactobacillus* and *Bifidobacteria* have no harmful effects.⁹

A limitation of this study was that the probiotic

used is a combination of species, hence, we could not determine which species best decreased nasal eosinophils in children with allergic rhinitis. Further studies that control for other confounding factors, such as food or milk that contained probiotics, are needed.

In conclusion, probiotic supplementation is beneficial for decreasing nasal eosinophils percentages in children with allergic rhinitis. Further study is needed to strengthen probiotic effects in children with allergic rhinitis.

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