ORIGINAL ARTICLE

Effects of Lactosucrose on Allergic Rhinitis from the Viewpoint of Changes in Intestinal Microbiota

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ABSTRACT

Background: **The purpose of this study was to investigate the effects of lactosucrose (LS) intake on the intestinal environment and on the improvement of allergic symptoms in patients with allergic rhinitis.**

Methods: **This study was conducted in a double-blind, parallel-group comparison study. Twenty-six subjects were divided into two groups, LS group and placebo group, and fed 7 g/day for 84 days. Stool and blood samples were collected before and after intake of LS, and the intestinal microbiota and IgE levels were analyzed. Changes in subjective symptoms were also investigated. The study period was 84 days from June 1, 2022.**

Results: **Subjective symptoms were unchanged in the LS group and significantly decreased in the placebo group. The LS group showed an increasing trend in the occupancy of *Bifidobacterium* spp. and a significant decrease in the occupancy of *Clostridium cluster IX* (P = 0.048) and *Lactobacillales* (P = 0.011).**

Conclusion: **When subjects with symptoms of nasal allergy were fed LS, a prebiotic, for 84 days, their intestinal microbiota improved. However, it did not affect IgE levels, an indicator of nasal allergy, and subjective symptoms.**

KEY WORDS

lactosucrose, allergic rhinitis, changes in intestinal microbiota, IgE

INTRODUCTION

Allergic rhinitis can be broadly classified into perennial allergic rhinitis and seasonal allergic rhinitis. Perennial allergic rhinitis is defined as one in which antigens are present throughout the year, such as mites, house dust, and dogs. Seasonal allergic rhinitis, on the other hand, is so-called hay fever, in which the amount of antigen changes with the seasons. Recently, the prevalence of allergic rhinitis in Japan is 49.2%[1)], and about one out of two people suffer from allergic rhinitis, including hay fever. Patients with allergic rhinitis experience nasal symptoms such as sneezing, runny nose, and nasal congestion, and ocular symptoms such as tearing, eye discharge, and itchy eyes, and these symptoms significantly reduce quality of life, such as poor concentration, discomfort, and insomnia. The number of patients with allergic rhinitis has been increasing, which has been increasing at a rate of approximately 10% per decade, thus increasing the importance of studying treatment methods for allergic rhinitis[2)]. In this study, we focused on lactosucrose (LS), which has the potential to reduce allergic symptoms by improving intestinal microbiota in subjects with allergic rhinitis, including hay fever. LS is a sweet-tasting food composed of lactose and sucrose. It is a non-digestible oligosaccharide that is hardly digested in the upper digestive tract, and is known to be selectively utilized by bifidobacteria[3)]. It has already been reported that LS intake inhibits IgE production in mice by increasing the occupancy of *Bifidobacterium bifidum* in the intestinal microbiota[4)]. In human studies, LS intake was reported to significantly reduce nasal and ocular symptoms caused by pollinosis[5)]. These findings suggest that intake of LS may bring about changes in the intestinal environment and suppress IgE production by the increased *Bifidobacterium bifidum*, reducing hay fever symptoms. Therefore, in this study, we evaluated how LS affects hay fever and observed changes in the intestinal environment.

SUBJECTS AND METHODS

Twenty-six subjects (3 males and 23 females) with symptoms of allergic rhinitis who gave consent were randomly divided into LS intake and placebo groups. The study period was 84 days starting June 1, 2022, and the LS group received 7 g/day of 70% LS manufactured by Harbor Laboratories, Inc. The evaluation items were subjective symptoms and severity, medications, defecation status, serum IgE levels, intestinal microbiota (T-RFLP analysis; MN-1 metho: TechnoSuruga Labs, Inc.), and dietary records. Allergy severity classification was based on the subject's own report, in accordance with the Rhinologic Allergy Treatment Guidelines 2020. The severity was classified according to the state of nasal obstruction: 0: asymptomatic, 1-5: mild, 6-10: moderate, 11-20: severe, and 21 or more: most severe. Subjects' pollen exposure during the study period was calculated based on cedar and cypress pollen data for 24 locations in Japan at the beginning of 2022 from the website of the NPO Pollen Information Association. Statistical analysis was conducted using IBM SPSS Statistics Ver. 24 (IBM Japan, Ltd.). Values are expressed as mean ± standard deviation. This study was reviewed and approved by the Ethical Review Committee of Kyoto Women's University. (*Approval number: 2021-31*)

Received on April 11, 2023 and accepted on April 13, 2023
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Table 1: Subject Background

	LS group	Placebo group	P-value (Comparison between two groups)
Age (years)	24.9 ± 10.8	20.9 ± 0.4	0.19
Severity	2.7 ± 0.9	2.4 ± 0.8	0.34
Total IgE level (U^A/ml)	191§ (10. 3637)†	325§ (34.2, 5677)†	0.98
Bifidobacterium spp. (%)	9.6 ± 8.1	12.1 ± 7.2	0.41

Mean ± SD

§: Median, †: (Min, Max)

(*p < 0.05)

Table 3: Changes in subjective symptoms

	group	Before Intervention (%)	After Intervention (%)	P-value (Before and after comparison)
Nasal symptoms	LS	2.9 ± 2.3	2.2 ± 2.1	0.133
	P	4.2 ± 2.3	1.9 ± 1.8	0.015*
Eye symptoms	LS	2.6 ± 1.6	1.7 ± 1.6	0.082
	P	2.2 ± 0.9	1.6 ± 1.0	0.007
Hindrance in daily life	LS	0.7 ± 0.9	0.4 ± 0.8	0.219
	P	1.4 ± 0.7	0.6 ± 0.8	0.011

(*p < 0.05)

RESULTS

1. Demographic characteristics and Allergic symptoms

Demographic characteristics and changes in IgE levels are shown in Table 1. In the LS group, the scores of nasal symptoms and degree of daily life disturbance decreased, but there was no significant difference. Ocular symptoms also decreased, with a significant trend. On the other hand, the placebo group showed a significant decrease in all scores for nasal symptoms, ocular symptoms, and degree of daily living disturbance.

2. Intestinal microbiota

Analysis of the intestinal microbiota before and after the LS and placebo groups revealed an increase in *Bifidobacterium spp.* in the LS group (P = 0.073), while there was no increase in *Bifidobacterium spp.* in the placebo group. *Clostridium cluster IX* and *Akkermansia* showed a significant decrease in the LS group (P = 0.048) and no decrease in the placebo group. The *Lactobacillales* group showed a significant decrease (p = 0.007) in the placebo group (Table 2).

3. Changes in IgE levels

No change was observed in total IgE levels, cedar-specific IgE levels decreased by 92.3% in the LS group and 83.6% in the placebo group, and cypress-specific IgE levels increased by 128.5% in the LS group and 100.4% in the placebo group, but none of the differences were significant. (Table 4).

4. Pollen exposure

The subjects lived in Shiga, Kyoto, and Osaka prefectures, and according to the NPO Pollen Information Association, cedar pollen dispersal in the Kinki region had not been observed since April 16, 2022 in Nishinomiya City, Hyogo Prefecture. The last time that cypress pollen was observed was on May 11, 2022, in Nishinomiya City, Hyogo Prefecture[6].

Table 2: Comparison of intestinal microflora analysis results

	group	Before Intervention (%)	After Intervention (%)	P-value (Before and after comparison)
Bifidobacterium	LS	9.6 ± 8.1	12.1 ± 7.2	0.073
	P	10.8 ± 5.6	9.0 ± 7.0	0.34
Lactobacillales	LS	2.4 ± 2.0	1.6 ± 0.6	0.16
	P	2.2 ± 0.9	1.6 ± 1.0	0.007*
Bacteroides	LS	31.8 ± 8.9	33.8 ± 10.0	0.59
	P	31.4 ± 8.5	32.8 ± 14.5	0.73
Clostridium cluster	LS	41.8 ± 11.9	38.0 ± 9.4	0.19
	P	41.2 ± 8.2	42.3 ± 9.9	0.60
Clostridium cluster IX (Negativicutes), Akkermansia	LS	4.9 ± 3.6	3.5 ± 2.1	0.048*
	P	4.0 ± 1.4	4.0 ± 3.4	0.99
Others	LS	13.0 ± 1.8	13.2 ± 2.3	0.74
	P	13.4 ± 2.7	13.6 ± 4.5	0.87

(*p < 0.05)

Table 4: Changes in IgE

	group	Before intervention (%)	After Intervention (%)	Amount of change (%)
Total IgE (UA/ml)	LS	191 (10, 3637)	179 (10, 5435)	104.9
	P	325 (40, 5677)	329 (29, 5516)	101.3
Japanese cedar-specific IgE (UA/ml)	LS	13.7 (0, 118)	12.4 (0, 120)	92.3
	P	24.3 (1.0, 85.4)	20.6 (1.8, 81.1)	83.6
Japanese cypress-specific IgE (UA/ml)	LS	6.4 (0, 97.3)	10.2 (0, 76.3)	128.5
	P	12.3 (0.4, 83.8)	13.9 (0.7, 80.9)	100.4

Median: (Min, Max)

DISCUSSION

This study was conducted in a double-blind comparative study. The grouping of patients into groups was appropriate because there were no differences in age, severity of illness, total IgE levels, or intestinal microbiota between the groups. Administration of LS did not change clinical symptoms of nasal allergy or IgE levels, but improved the intestinal environment.

Regarding changes in the intestinal microbiota, *Bifidobacterium* spp. showed an increasing trend from 9.6 ± 8.1% to 12.1 ± 7.2% in the LS group (p = 0.073). Clostridium cluster IX, *Akkermansia* genus showed a significant decrease from 4.9 ± 3.6% to 3.5 ± 2.1% (P = 0.048). *Bifidobacterium* suppresses the production of putrefactive and harmful bacteria and stimulates the immune function of the organism[7], thereby In the placebo group, *Lactobacillales* significantly decreased from 2.2 ± 0.9% to 1.6 ± 0.6% (P = 0.011). *Lactobacillales* have been reported to have beneficial effects such as intestinal regulation and infection prevention[8]. Based on the above, it can be said that the intestinal environment tended to improve with LS intake. Therefore, it can be said that the intake of LS in this study improved the intestinal microbiota, but was not effective in improving serum IgE levels and subjective symptoms related to nasal allergy.

In the Kinki region, cedar pollen dispersion was not observed in Nishinomiya City, Hyogo Prefecture, until April 16, 2022, and cypress pollen dispersion was not observed in the same city until May 11, 2022. Since the study began on June 1, subjects were not exposed to cedar or cypress pollen during the study period; the change in specific IgE for cedar pollen that ended in April was 92.3% in the LS group and 83.6% in the P group, and the change in specific IgE for cypress pollen that ended in May was 128.5% in the LS group was 128.5% and 100.4% for the P group, indicating that the effect of the LS intake remained. This result was not due to the effect of LS intake, but rather to the seasonal pollen dispersal. The lack of significant changes in serum IgE levels suggests that the 12-week intake of the test food in this study may not have been sufficient time for serum IgE levels to decrease. Ido *et al*. reported a significant decrease in serum IgE levels in a study in which 12 pollinosis patients were administered LS for 52 weeks[9)]. On the other hand, according to Kato *et al*., Bifidobacterium BB536 was taken for 8 weeks from June to September to examine the improvement of nasal allergies due to changes in the intestinal environment, but total IgE levels increased in both the intake and placebo groups[10)]. This study, like the present study, was conducted after June, when pollen dispersal ends. These findings suggest that seasonal environmental changes, such as differences in the amount of pollen dispersal before and after the start of the study for a study period of less than one year, may have an effect. However, it can be said that the test foods can be examined without being affected by seasonal changes in pollen dispersal amounts by taking the foods for one year. It is also possible that continuous intake for more than 12 weeks is necessary to obtain sufficient effect of LS as prebiotics on changes in the intestinal microbiota. Regarding changes in subjective symptoms, Sadakiyo *et al*. reported a significant reduction in both nasal and ocular symptoms after 19 weeks of LS intake. The study period was set from January to May, when cedar and cypress pollen dispersal occurs, and weekly questionnaires were administered to follow the progress of the subjects during the period. In the future, we would like to increase the number of subjects, consider the season, survey period, etc., and continue further research.

CONCLUSION

After 84 days of LS, a prebiotics, intake, the intestinal microbiota of subjects with nasal allergy symptoms increased the occupancy of Bifidobacterium spp. and decreased the occupancy of Clostridium clusters. This indicates that the intestinal environment tended to improve with LS intake. However, there was no improvement in IgE levels, an indicator of nasal allergies. The decrease in subjective symptoms was probably due to a decrease in the amount of pollen in the air, and this study could not prove that LS had an effect on the improvement of nasal allergies. The absence of effect at 12 weeks in the present study also suggests a relationship with the duration of LS intake.

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