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## **Clinical observation of active probiotics in the treatment of allergic rhinitis and analysis of its effect on immunoregulation**

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The clinical incidence rate of allergic rhinitis is high. Allergic rhinitis is an immunoglobulin E-induced type allergic diseases with classic clinical symptoms. It severely influences patients' quality of life<sup>[1-2]</sup>. Antihistamines are an effective means for treating allergic rhinitis. Such drugs can significantly improve patients' clinical symptoms<sup>[3]</sup>. Recent studies found that active probiotics can regulate the immune functions of allergic rhinitis patients, showing clinical benefits for improving prognosis<sup>[4-5]</sup>. In this study, we added an adjuvant therapy of active probiotics containing *Lactobacillus paracasei*, *Lactobacillus reuteri*, and *Lactobacillus rhamnosus* to the clinical treatment of persistent allergic rhinitis patients. The clinical outcomes were satisfactory. A full account is presented in the following sections.

### 1. Data and methodology

#### 1.1 General data

A total of 120 patients with persistent allergic rhinitis treated at the research hospital between June 2015 and June 2016 were examined. They were randomly allocated to a probiotics group and a control group according to the order of admission. Each group comprised 60 patients. The probiotics group comprised 38 male patients and 22 female patients. They were between the ages of 18 and 60 ( $35.45 \pm 6.47$ ). The duration of illness was between one and 24 ( $7.15 \pm 1.33$ ) years. The control group comprised 37 male patients and 23 female patients. They were between the ages of 18 and 60 ( $35.48 \pm 6.33$ ). The duration of illness was between one and 24 ( $7.13 \pm 1.35$ ) years. A comparison of the

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gender proportion, age composition, and illness duration of the two groups yielded no significant statistical differences ( $P>0.05$ ), validating that the two groups were comparable.

## 1.2. Inclusion and exclusion criteria

Inclusion criteria: Patients must meet the diagnosis criteria for persistent allergic rhinitis stipulated in the *Guidelines for the Diagnosis and Treatment of Allergic Rhinitis*<sup>[6]</sup> and confirmed by routine examinations and serum-specific IgE tests combined with clinical manifestations and have not undergone other drug treatments within four weeks of admission. Exclusion criteria: Complicated with other severe primary illnesses; blood system or immune system diseases; allergies to the drugs used in this study; and cannot comply with the full treatment period and follow-up.

## 1.3 Methodology

The patients in the control group received routine antihistamine therapy: 10 mg of cetirizine (Shanghai Qingsong Pharmacy Limited Company; Approval number: H20080307; Specifications: 5 mg) administered orally once a day conditionally accompanied by RHINOCORT® Allergy Spray (AstraZeneca AB; License: H20110259; Specifications: 32 µg/dose) once a day for 12 weeks.

The patients in the probiotics group were prescribed with the same antihistamine therapy as those in the control group, with the addition of one sachet of probiotics (Ming Li Ting manufactured by HK Good Ally Biotechnology Co. Ltd.; Primary ingredients: Lactobacillus paracaseiGL-156, Lactobacillus reuteriGL-104, and Lactobacillus rhamnosusMP-108; Bacterial ingredients produced by glac Biotech Co., Ltd.) three times a day taken with warm water on an empty stomach for 12 weeks.

## 1.4 Evaluation indicators

The clinicalefficacy of the two groups was compared at the end of the treatment period. The pre-treatment and post-treatment immune indicators levels [serum total IgE (TIgE), specific IgE

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(sIgE), and interleukin-4 (IL-4)] and significant improvement time of symptoms and signs of the two groups of patients were measured.

## 1.5 Clinical efficacy evaluation

The *Guidelines for the Diagnosis and Treatment of Allergic Rhinitis* was referenced for scoring the patients' symptoms and signs, including nasal congestion, runny nose, sneezing, and nasal examination. The items were scored on a scale of 1 to 3, and the scores of the four items were summed. Clinical efficacy evaluation criteria<sup>[7]</sup>: Very effective: Overall treatment score for symptoms and signs reduced by 50% or more; effective: overall treatment score for symptoms and signs reduced between 20% and 50%; ineffective: failure to comply with the preceding criteria. Overall efficacy=very effective+effective.

The UniCAP fluorescent-linked immunosorbent assay was used to measure serum TlgE and sIgE levels. ELISA was used to measure serum IL-4 levels.

## 1.6 Statistical analysis



The IBM SPSS Statistics 22 software was used for statistical analysis. The measurement data were presented as ( $\bar{x} \pm s$ ) and compared using *t*-tests. The enumeration data were compared using  $\chi^2$  tests.  $P < 0.05$  was adopted as the measure of statistical significance.

## 2. Results

### 2.1. A comparison of the clinical efficacy of the two groups.

The overall efficacy of the probiotics group was higher than that of the control group. The results achieved significant statistical differences ( $P < 0.05$ ), as tabulated in Table 1.

Table 1. A comparison of the clinical efficacy of the two groups [n (%)]

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Group	<i>n</i>	Very effective	Effective	Ineffective	Overall efficacy
Probiotics group	60	36 (60.00)	20 (33.33)	4 (6.67)	56 (93.33)*
Control group	60	29 (48.33)	19 (31.67)	12 (20.00)	48 (80.00)
$\chi^2$					4.615
<i>P</i>					0.032

Note: Compared to the control group, \* $P < 0.05$

## 2.2. A comparison of the immune indicator levels of the two groups before and after treatment

The post-treatment serum TIgE, sIgE, IL-4 levels of both groups were significantly lower than those before treatment. The results achieved significant statistical differences ( $P < 0.05$ ). The post-treatment serum TIgE, sIgE, IL-4 levels of the patients in the probiotics group were significantly lower than those in the control group. The results achieved significant statistical differences ( $P < 0.05$ ), as tabulated in Table 2.

Table 2. A comparison of the immune indicator levels of the two groups before and after treatment ( $\bar{x} \pm s$ )

Group	<i>N</i>	Time	TIgE (IU/L)	sIgE (KUA/L)	IL-4 (pg/L)
Probiotics group	60	Before treatment	396.44±32.47	28.45±6.61	110.22±27.37
		After treatment	138.38±12.47 $\Delta^*$	15.33±4.47 $\Delta^*$	32.49±5.53 $\Delta^*$
		<i>t</i>	9.859	4.022	7.137
		<i>P</i>	0.001	0.022	0.001
Control group	60	Before treatment	394.58±33.05	28.42±6.39	110.09±26.88
		After treatment	167.75±15.44 $\Delta$	19.86±4.85 $\Delta$	50.44±6.77 $\Delta$
		<i>t</i>	9.822	4.008	7.051
		<i>P</i>	0.001	0.026	0.001
<i>t</i> <sub>both groups after</sub>			7.293	4.602	4.545

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treatment					
$P$ both groups after treatment			0.015	0.020	0.018

Note: Compared to the same group before treatment,  $\Delta P < 0.05$ ; Compared to the control group,  $*P < 0.05$

## 2.3 A comparison of the significant improvement times of symptoms and signs of the two groups

The significant improvement times of paroxysmal sneezing, water-like nasal mucus, nasal itching, and nasal congestion of the patients in the probiotics group were significantly shorter than those in the control group. The results achieved significant statistical differences ( $P < 0.05$ ), as tabulated in Table 3.

Table 3. A comparison of the significant improvement times of symptoms and signs of the two groups ( $\bar{x} \pm s$ , d)

Group	$N$	Paroxysmal sneezing	Water-like nasal mucus	Nasal itching	Nasal congestion
Probiotics group	60	$11.46 \pm 3.17^*$	$12.05 \pm 3.49^*$	$10.88 \pm 3.05^*$	$11.52 \pm 3.43^*$
Control group	60	$14.85 \pm 3.66$	$15.15 \pm 3.88$	$14.22 \pm 3.81$	$14.77 \pm 3.55$
$t$		3.097	3.288	3.369	3.028
$P$		0.030	0.025	0.028	0.034

Note: Compared to the control group,  $*P < 0.05$

## 3 Discussion

Allergic rhinitis is an immunoglobulin E-induced type allergic disease. Disease progression involves a number of immunocompetent cells and cytokines. Classic clinical symptoms include nasal itching, sneezing, and runny nose. A number of cases are accompanied by hyposmia<sup>[8]</sup>. A previous

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clinical report mentioned that allergic rhinitis is a multifactorial disease induced by the interaction between genes and the environment. Genetic factors and the exposure to allergens (e.g., mites, pollen, animal dander, fungi, cockroaches, and food) may trigger an onset<sup>[9]</sup>. The malignancy of allergic rhinitis alone is relatively low. However, conditions exacerbate when allergic rhinitis is accompanied by asthma, conjunctivitis, chronic rhinosinusitis, or adenoid hypertrophy, significantly influencing patients' quality of life. Therefore, quickly controlling clinical symptoms are crucial.

Clinical treatment of allergic rhinitis can be generalized into two aspects. The first aspect is isolation from allergens. The second is drug treatment, immunotherapy, and surgery. Surgery is only considered when patients are unresponsive to drug treatment or immunotherapy, exhibit visible anatomical abnormalities or dysfunction in the nasal cavity, or have chronic rhinosinusitis or nasal polyps. Therefore, the scope of clinical application is small. Immunotherapy entails the use of allergen vaccines or long-term subcutaneous injection or sublingual application of immunologic drugs to induce clinical and immune tolerance. These approaches often cause localized or systemic adverse reactions and are generally prescribed to patients who are unresponsive to routine drug treatment. Drug treatment is a standard treatment approach adopted in clinical practice. Antihistamines, glucocorticoids, anti-leukotrienes, color ketones, intranasal decongestants, and intranasal anticholinergics can effectively control the clinical symptoms of allergic rhinitis<sup>[10-11]</sup>. These drugs are typically administered orally or via the nasal cavity. Among which, antihistamines are the preferred drugs for treating allergic rhinitis. It is worth noting that effects cannot persist for long once drug treatment is suspended. Therefore, maintenance therapy is required<sup>[12]</sup>. The cetirizine applied in this study is a first-generation active hydroxy acid metabolite of the H1-receptor hydroxyzine. It has a strong preference for peripheral H1 receptors. Therefore, it can effectively improve the clinical symptoms of allergic rhinitis. Animal trials validated that cetirizine had no significant anticholinergic and anti-serotonin effects. It is unlikely to pass the blood-cerebrospinal fluid barrier and act on central H1 receptors. Hence, the clinical application of cetirizine is safe and has minimal effects on the nervous system<sup>[13]</sup>. Research findings suggest that the overall treatment efficacy of the control group

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was 80.00% with significant improvement in serum TlgE,sIgE, and IL-4 levels after treatment, validating the effectiveness of antihistamine therapy.

In recent years, adjuvant probiotics therapy has shown to have positive clinical effects for the treatment of inflammation and allergies<sup>[14]</sup>. A previous study found that probiotics significantly improved patients' microbiological balance and immune functions<sup>[15]</sup>. Ozturk AB et al.<sup>[16]</sup> examined 32 allergic rhinitis patients who underwent probiotics therapy and found that the patients achieved different levels of TlgEand sIgE reduction and exhibited significant improvement in the clinical symptoms of paroxysmal sneezingand water-like nasal mucus. Koa EA et al.<sup>[17]</sup> validated that the intake of active probiotics facilitated the recovery of the immune functions of patients with allergic diseases, regulated microorganisms in the patients' bodies, improved Th1/Th2 balance and corrected intestinal flora disorder, ultimately alleviating allergic symptoms. The probiotics used in this study comprised *Lactobacillus paracasei*, *Lactobacillus reuteri*, and *Lactobacillus rhamnosus*. Results indicated that the post-treatment serum TlgE,sIgE, and IL-4 levels of the patients in the probiotics group were significantly lower than those in the control group. These results were consistent with those proposed in previous studies. The overall treatment efficacy of the patients in the probiotics group was significantly higher than that of the control group. The results achieved significant statistical differences ( $P<0.05$ ). The significant improvement times for paroxysmal sneezing, water-like nasal mucus, nasal itching, and nasal congestion of the patients in the probiotics group were significantly shorter than those in the control group. The results achieved significant statistical differences ( $P<0.05$ ). These results were associated with the fact that the probiotics improve the body's immune functions, accelerates the recovery from allergic rhinitis symptoms, and enhances anti-inflammatory effects.

In conclusion, the effects of active probiotics for treating allergic rhinitis is clinically beneficial. It effectively improves patients' immune indicators and shortens recovery times. Therefore, they should be promoted.

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