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Original Article

Clinical efficacy of jade wind-barrier powder combined with loratadine in the treatment of pediatric allergic rhinitis

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Abstract: Objective: To investigate the clinical efficacy of Jade Wind-Barrier Powder combined with Loratadine in the treatment of pediatric allergic rhinitis (PAR). Methods: The clinical data of 101 children with allergic rhinitis (AR) admitted to the Affiliated Hospital of Qingdao University and Affiliated Hospital of Nanjing University of Traditional Chinese Medicine from January 2019 to December 2019 were retrospectively analyzed. The children were randomly divided into Group A (n=50) and Group B (n=51) in accordance with a random number table. Group A was treated with Loratadine only, while Group B was treated with Loratadine combined with Jade Wind-Barrier powder. The clinical efficacy, symptom disappearance time, symptom scores before and after treatment, indices of immunological function, changes in the indices of inflammatory factors and disease recurrence were compared between the two groups. Results: The overall response rate (ORR) in Group B (96.08%) was higher than that in Group A (76.00%) ($P < 0.05$). The disappearance time of sneezing, stuffy nose, runny nose and itchy nose in Group B was shorter than that in Group A ($P < 0.05$). After treatment, Group B exhibited lower symptom scores for sneezing, stuffy nose, runny nose and itchy nose, lower levels of IL-13, IL-4 and TNF-α, and higher $CD4^+CD25^+$, $CD19^+$ and $CD8^+$ than Group A ($P < 0.05$). The recurrence rate in Group B (3.92%) was lower than that in Group A (26.00%) ($P < 0.05$). Conclusion: Jade Wind-Barrier powder combined with Loratadine can improve clinical symptoms, immunity, inflammation levels and disease recurrence rate of PAR patients, with a significant clinical efficacy.

Keywords: Jade wind-barrier powder, loratadine, adjuvant treatment, children, allergic rhinitis, efficacy

Introduction

Clinically, pediatric allergic rhinitis (PAR), also known as allergic rhinitis (AR), is a chronic inflammatory disease characterized by nasal mucosal congestion, which has a very high incidence [1]. The main clinical symptoms of AR include sudden cough at night, postnasal drip, nasal congestion, nasal discharge, sneezing and itchy nose [2]. AR has a complex pathogenesis. Currently, it is generally believed that the pathogenesis of AR is related to the exposure of indoor and outdoor allergens and the genetic allergic constitution, and AR mainly occurs in the winter and spring and easily recurs [3].

Currently, physical therapy, antihistamines, decongestants, anti-inflammatory agents, anticholinergic drugs, immunotherapy and leukotriene receptor antagonists are commonly applied for the treatment of APR, and the therapeutic effects of different therapeutic methods are quite different [4, 5]. Loratadine is a second-generation antihistamine drug mainly used to treat multiple allergic symptoms [6]. Compared with the first-generation antihistamine drugs, Loratadine does not cause drowsiness, and has been widely used in the treatment of pollinosis, allergic conjunctivitis, chronic or acute urticaria, and AR [7, 8]. Although Loratadine exhibits a clinical efficacy in treating PAR, the effect of

Loratadine alone remains to be improved [9]. In traditional Chinese medicine (TCM), PAR is classified into the category of "Sniveling Nose". It is believed that PAR occurs as a result of debilitation of lung Qi, insecurity of the defensive exterior, and invasion of nose orifices, resulting in nasal discharge and sneezing. Over these years, TCM therapy has been widely used as the adjuvant treatment of AR, and has achieved satisfactory intervention effects [10].

Jade Wind-Barrier Powder is a classic prescription for invigorating Qi and consolidating the foundation and has been widely used in clinical practice in China; it is composed of Radix Saposhnikoviae, Rhizoma Atractylodis Macrocephalae, and Radix Astragali seu Hedysari, and has the function of strengthening vital Qi to eliminate pathogenic factor and invigorating Qi and consolidation of the exterior [11]. Based on Loratadine, Jade Wind-Barrier Powder was implemented as the adjuvant treatment in this study, so as to further improve the therapeutic effects on the treatment of PAR, the body's immunity, and multiple clinical symptoms and signs of PAR patients.

Materials and methods

Clinical data

The clinical data of 101 PAR patients admitted to the Affiliated Hospital of Qingdao University and Affiliated Hospital of Nanjing University of Traditional Chinese Medicine from January 2019 to December 2019 were retrospectively analyzed. The children were randomly divided into Group A (n=50) and Group B (n=51) in accordance with a random number table. Group A was treated with Loratadine only, while Group B was treated with Loratadine combined with Jade Wind-Barrier Powder. (1) Inclusion criteria: patients diagnosed with PAR; those without contraindications to the study drugs; and those who were aged 3-12 years. Informed consent was signed by the patients' families. This study obtained the approval from the Ethics Committee of the Affiliated Hospital of Qingdao University. (2) Exclusion criteria: rhinitis induced by viruses, mycoplasma and bacteria; patients complicated with hepatic and renal dysfunction; those treated with hormone drugs or immunosuppressants within one month before enrollment; those complicated with severe infections; and those complicated with autoimmune diseases.

Methods

Group A: the children were given Loratadine orally (approval number: SFDA approval number: H20041044, manufacturer: Grand Pharmaceutical (China) Co., Ltd., specifications: 10 mg * 7 pcs). The children weighing > 30 kg took 10 mg once a day, while the children weighing ≤ 30 kg took 5 mg once a day for 4 weeks.

Group B: Loratadine was taken in the same way as that in Group A. The children were additionally treated with Jade Wind-Barrier Powder. Jade Wind-Barrier Powder, Sanjiu decocting-free granules, 20 g of Radix Astragali seu Hedysari (2 bags), 20 g of Rhizoma Atractylodis Macrocephalae (2 bags), and 10 g of Radix Saposhnikoviae (1 bag) were prepared as a dose of medicine. The children aged 3-6 years took a dose of medicine per 1.5 d; the children aged 7-12 years took a dose of medicine per day, or took each dose of medicine using 200 ml of hot water; the children aged 3-6 years took a dose of medicine using 50 ml of hot water each time, twice a day, and the children aged 7-12 years took a dose of medicine using 100 ml of hot water each time, twice a day for 4 weeks.

Observational indices

(1) Efficacy assessment criteria [12]: After treatment, sneezing, nasal congestion, runny nose, itchy nose and other symptoms basically disappeared. The results of nasal endoscopy showed that there was no secretion and edema in the turbinate, and the nasal mucosa was ruddy, indicating a marked response. After treatment, the clinical symptoms were alleviated. The results of nasal endoscopy suggested that slight edema occurred in the turbinate and the nasal mucosa was dark red, indicating a moderate response. After treatment, the clinical symptoms remained unchanged, or even worsened, indicating no response. Overall response = moderate response + marked response.

(2) Symptom disappearance time: The symptom disappearance time was compared between the two groups.

Table 1. Comparison of general data between the two groups [n (%)]/(mean ± SD)

Data		Group A (n=50)	Group B (n=51)	t/X^2	*P*
Sex (cases)	M	27 (5400)	29 (56.86)	0.084	0.773
	F	23 (46.00)	22 (43.14)		
Age (years)		6.18±0.28	6.22±0.22	0.799	0.426
Severity of illness (cases)					
Mild		31 (62.00)	32 (62.75)	0.025	0.998
Moderate		18 (36.00)	17 (33.33)		
Severe		1 (2.00)	2 (3.92)		

Table 2. Comparison of clinical efficacy between the two groups [n (%)]

Group	Number of cases	Marked response	Moderate response	No response	ORR
Group A	50	21 (42.00)	17 (34.00)	12 (24.00)	38 (76.00)
Group B	51	36 (70.59)	13 (25.49)	2 (3.92)	49 (96.08)*
X^2					8.525
P					0.004

Note: *indicates the comparison with Group A, $P < 0.05$.

(3) Symptom scores [13]: Before and after treatment, based on the severity of sneezing, stuffy nose, runny nose and itchy nose, the assessment was conducted using a score of 1-3 points. A higher score indicates more serious symptoms.

(4) Immunologic function [14]: Before and after treatment, 2 ml of fasting venous blood was drawn from the children in the two groups, and centrifuged for 10 min at a speed of 3000 r/min. $CD4^+CD25^+$, $CD19^+$ and $CD8^+$ T cell subsets were measured by flow cytometry.

(5) Inflammatory factors [15]: Before and after treatment, 2 ml of fasting venous blood was drawn from the children in the two groups, and centrifuged at a speed of 3000 r/min for 10 min. The levels of IL-13, IL-4 and TNF-α were measured by enzyme-linked immunosorbent assay (ELISA).

(6) Disease recurrence: At 6 months after treatment, the conditions of disease recurrence were compared between the two groups.

Statistical analysis

SPSS 22.0 was adopted for statistical analysis. The measurement data were expressed as mean ± standard deviation (mean ± SD). The data conforming to a normal distribution were detected by *t* test, and those not conforming were detected by Mann-Whitney U test. The enumeration data were expressed as [n (%)], and the comparison of enumeration data between groups was carried out by chi-aquared test. $P < 0.05$ indicated a statistical significance.

Results

Comparison of general data between the two groups

There was no significant difference in terms of gender, age, and severity of conditions between the two groups ($P > 0.05$) (**Table 1**).

Comparison of clinical efficacies between the two groups

After treatment, there were 21 cases with a marked response, 17 cases with a moderate response and 12 cases with no response in Group A; and 36 cases with a marked response, 13 cases with a moderate response and 2 cases with no response in Group B. The overall response rate (ORR) in Group B (96.08%) was higher than that in Group A (76.00%) ($P < 0.05$) (**Table 2**).

Comparison of symptom disappearance time between the two groups

The disappearance time of sneezing, nasal congestion, runny nose and itchy nose in Group B (4.12±0.15 d, 1.08±0.22 d, 2.12±0.18 d, and 1.52±0.15 d) was shorter than that in Group A ($P < 0.05$) (**Figure 1**).

Comparison of symptom scores between the two groups

There was no remarkable difference in the symptom scores between the two groups before treatment ($P > 0.05$). Compared with those before treatment, the scores of sneezing, stuffy nose, runny nose and itchy nose were decreased in the two groups after treatment (*P*

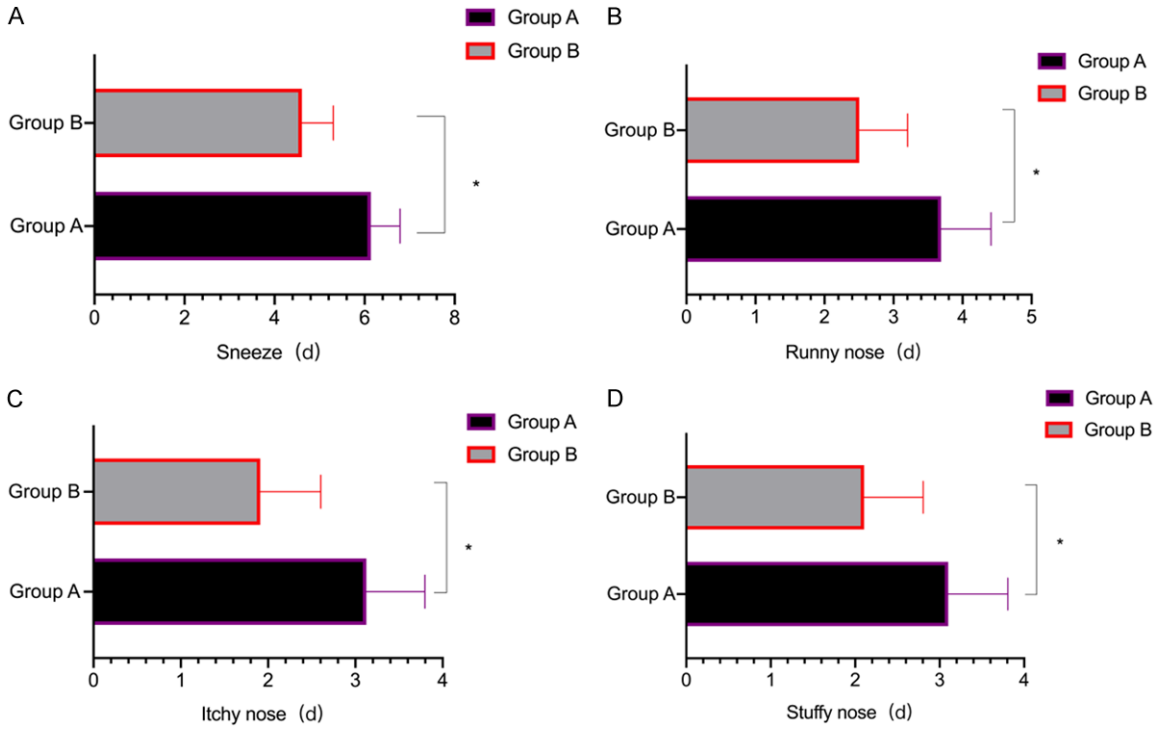

Figure 1. Comparison of symptom disappearance time between the two groups. (A) shows that the disappearance time of sneezing in Group B was shorter than that in Group A after treatment ($P < 0.05$). (B) suggests that the disappearance time of nasal congestion in Group B was shorter than that in Group A after treatment ($P < 0.05$). (C) demonstrates that the disappearance time of runny nose in Group B was shorter than that in Group A after treatment ($P < 0.05$). (D) reveals that the disappearance time of itchy nose in Group B was shorter than that in Group A ($P < 0.05$). *indicates the comparison with Group A, $P < 0.05$.

< 0.05). The scores of sneezing, stuffy nose, runny nose and itchy nose in Group B were lower than those in Group A after treatment ($P < 0.05$) (**Figure 2**).

Comparison of indices of immunologic function between the two groups

Before treatment, there was no marked difference in the indices of immunologic function between the two groups ($P > 0.05$). Compared with those before treatment, the levels of $CD4^+CD25^+$, $CD19^+$ and $CD8^+$ were increased in both groups after treatment ($P < 0.05$). The levels of $CD4^+CD25^+$, $CD19^+$ and $CD8^+$ in Group B were higher than those in Group A after treatment ($P < 0.05$) (**Figure 3**).

Comparison of indices of inflammatory factors between the two groups

Before treatment, there was no remarkable difference in the index levels of inflammatory factors between the two groups ($P > 0.05$). Compared with those before treatment, the levels of IL-13, IL-4 and TNF-α were decreased in the two groups after treatment ($P < 0.05$). The levels of IL-13, IL-4 and TNF-α in Group B were lower than those in Group A after treatment ($P < 0.05$) (**Figure 4**).

Comparison of disease recurrence between the two groups

At 6 months after treatment, there were 2 cases with the disease recurrence in Group B, and 13 cases with the disease recurrence in Group A. The recurrence rate in Group B (3.92%) was significantly lower than that in Group A (26.00%) ($P < 0.05$) (**Table 3**).

Discussion

Dust mites abound in human living conditions, and their metabolites and excretions are highly allergic, thus easily inducing AR [16]. Therefore, AR, as one of the common diseases in otolaryngology, poses a great challenge to treatment [17]. Currently, drug symptomatic therapy is mainly adopted for the clinical treatment of AR.

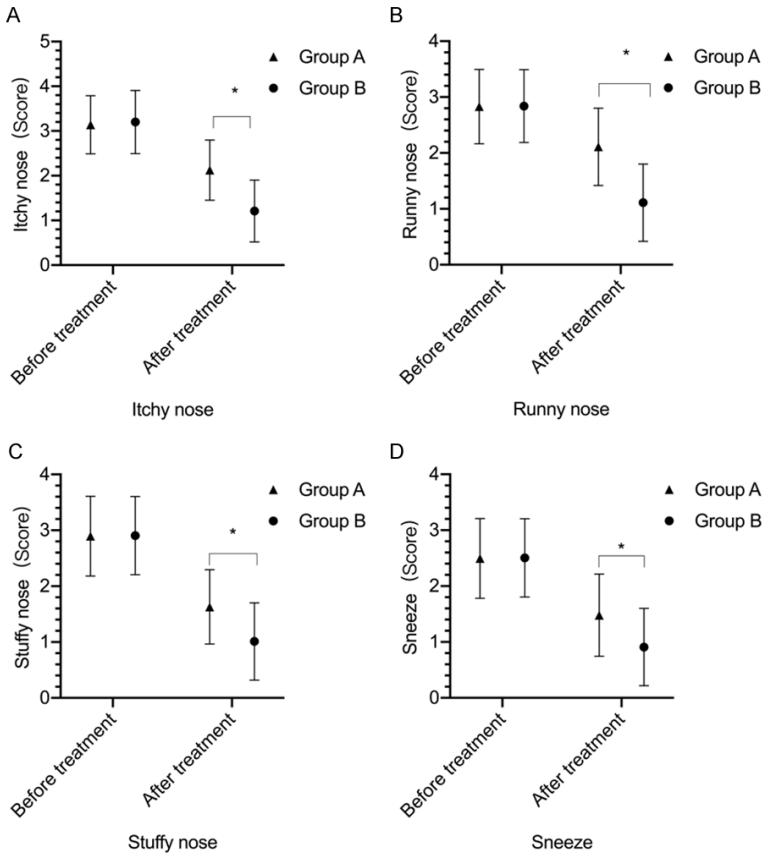

Figure 2. Comparison of symptom scores between the two groups. (A) shows the comparison of the scores for itchy nose between the two groups before treatment ($P > 0.05$), and the score for itchy nose in Group B was lower than that in Group A after treatment ($P < 0.05$). (B) suggests the comparison of the scores for runny nose between the two groups before treatment ($P > 0.05$), and the score for runny nose in Group B was lower than that in Group A after treatment ($P < 0.05$). (C) shows the comparison of the scores for stuffy nose between the two groups before treatment ($P > 0.05$), and the score for stuffy nose in Group B was lower than that in Group A after treatment ($P < 0.05$). (D) reveals the comparison of the scores for sneezing between the two groups before treatment ($P > 0.05$), and the score for sneezing in Group B was lower than that in Group A after treatment ($P < 0.05$). *indicates the comparison with Group A, $P < 0.05$.

The common therapeutic drugs include mast cell membrane stabilizers, leukotriene receptor antagonists, antihistamines and glucocorticoids [18, 19]. Loratadine, an H1 receptor blocker, can inhibit histamine release from mast cells and increase capillary permeability, thereby alleviating allergic symptoms and exerting anti-allergic effects [20]. Although Loratadine is clinically effective in treating PAR, it is difficult to maintain a long-term drug concentration. For this reason, there is a high recurrence rate, and the immunologic and hepatic and renal functions of the body may be affected to varying degrees after discontinuing Loratadine. Therefore, the efficacy of Loratadine alone needs to be further improved [21, 22].

In TCM, PAR is classified into the category of "Sniveling Nose". It is believed that nose is the opening of lung, so the onset of sniveling nose is usually attributable to the lung [23]. Exogenous wind and cold of the body cause the dysfunction of lung Qi, resulting in non-diffusion of lung Qi, stagnation in the nose orifice, and thus inducing AR [24]. Therefore, AR is characterized by the vacuity-repletion complex and root vacuity and tip repletion. Tip repletion indicates wind-cold dampness and water toxin, while root vacuity indicates the deficiencies of kidney, spleen, and lung Qi. Although AR occurs in the lung, the onset of AR is closely related to kidney and spleen. Therefore, it is necessary not only to clear the nasal orifices and warm the lung and dissipate cold, but also secure the kidney and safeguard the stomach in the treatment of AR. In view of this, Loratadine combined with Jade Wind-Barrier Powder was applied to treat PAR. The results showed that Group B was superior to Group A regarding the ORR, for time to symptom relief, TCM symptom scores and disease recurrence rate. This exhibited that Loratadine combined with Jade Wind-Barrier Powder was conducive to improving the clinical symptoms and reducing the disease recurrence rate, exhibiting a significant clinical efficacy. Wu et al. also found that the total effective rate of Loratadine combined with Jade Wind-Barrier granules in the treatment of PAR was higher than that of the single Loratadine group, and the disease recurrence rate and the incidence of adverse reactions were lower than that in the

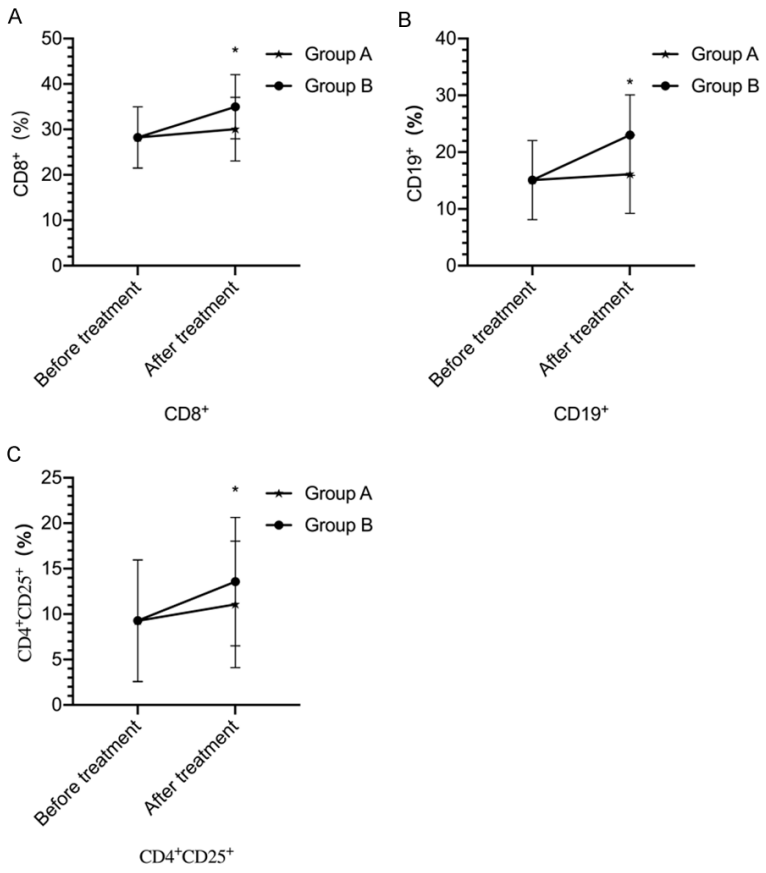

Figure 3. Comparison of indices of inflammatory factors between the two groups. (A) shows the comparison of the levels of $CD8^+$ between the two groups before treatment ($P > 0.05$), and the level of $CD8^+$ in Group B was higher than that in Group A after treatment ($P < 0.05$). (B) suggests the comparison of the levels of $CD19^+$ between the two groups before treatment ($P > 0.05$), and the level of $CD19^+$ in Group B was higher than that in Group A after treatment ($P < 0.05$). (C) reveals the comparison of the levels of $CD4^+CD25^+$ between the two groups before treatment ($P > 0.05$), and the level of $CD4^+CD25^+$ in Group B was higher than that in Group A after treatment ($P < 0.05$). *indicates the comparison with Group A, $P < 0.05$.

single Loratadine group [25], which was highly consistent with the results of this study. The investigation of its mechanism of action revealed that Jade Wind-Barrier Powder, which is composed of Radix Saposhnikoviae, Rhizoma Atractylodis Macrocephalae, and Radix Astragali seu Hedysari, is a classic prescription for boosting Qi and securing the root and supporting healthy energy to eliminate evils. Rhizoma Atractylodis Macrocephalae can boost Qi and fortify the spleen, and its combination with Radix Astragali seu Hedysari can strengthen the effect of boosting Qi and securing the root, prevent and expel wind to relieve convulsions, and relieve exterior syndrome by dispersion. The combination of Rhizoma Atractylodis Macrocephalae and Radix Saposhnikoviae can dissipate wind and resist evil, and does not damage healthy energy. Jade Wind-Barrier Powder can boost Qi and secure the root, and support healthy energy to eliminate evils [26]. Currently, clinical studies demonstrated that the release of non-infectious inflammatory factors caused by IgE are the main pathogenesis of AR [27]. Additionally, the imbalance of B lymphocyte and T lymphocyte subsets plays a pivotal role in the occurrence and progression of AR. In this study, the levels of $CD4^+CD25^+$, $CD19^+$ and $CD8^+$ in Group B were higher than those in Group A after treatment, suggesting that Loratadine combined with Jade Wind-Barrier Powder can improve the body's immunity in PAR patients. The investigation of its mechanism of action revealed that $CD8^+$ inhibited T lymphocytes, and the marked decrease in the level of $CD8^+$ may be one of the main pathogenesis of AR. $CD4^+CD25^+$ regulatory T lymphocytes can effectively regulate Th1/Th2 balance, thereby alleviating AR symptoms. $CD19^+$ can regulate the proliferation and activation of B lymphocytes, and the activated B lymphocytes can trigger an inflammatory reaction through regulating IgE level [28]. In this study, the levels of $CD4^+CD25^+$, $CD19^+$ and $CD8^+$ in Group B were higher than those in Group A after treatment, suggesting that Jade Wind-Barrier Powder had a satisfactory therapeutic effect. Inflammation plays a significant role in the onset of AR. After treatment, the levels of IL-13, IL-4 and TNF-α in Group B were lower than those in Group A, indicating that Loratadine combined with Jade Wind-Barrier Powder could alleviate the inflammatory reactions of PAR patients. The investigation of its mechanism of action showed that TNF-α mediated multiple pathological processes (*e.g.*, extracellular

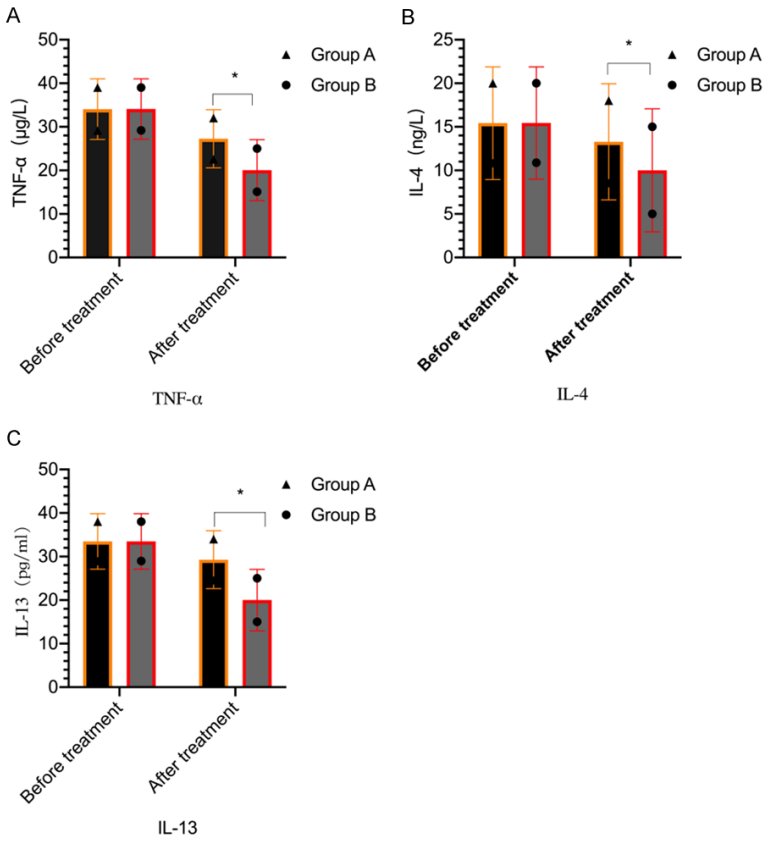

Figure 4. Comparison of indices of inflammatory factors between the two groups. (A) shows the comparison of the levels of TNF-α between the two groups before treatment ($P > 0.05$), and the level of TNF-α in Group B was lower than that in Group A after treatment ($P < 0.05$). (B) suggests the comparison of the levels of IL-4 between the two groups before treatment ($P > 0.05$), and the level of IL-4 in Group B was lower than that in Group A after treatment ($P < 0.05$). (C) reveals the comparison of the levels of IL-13 between the two groups before treatment ($P > 0.05$), and the level of IL-13 in Group B was lower than that in Group A after treatment ($P < 0.05$). *indicates the comparison with Group A, $P < 0.05$.

Table 3. Comparison of conditions of disease recurrence between the two groups [n (%)]

Group	Number of cases	Recurrence rate
Group A	50	13 (26.00)
Group B	51	2 (3.92)*
X^2		13.299
P		0.000

Note: *indicates the comparison with Group A, $P < 0.05$.

matrix formation, fibroblast proliferation and leukocyte chemotactic activation), thus worsening the conditions. IL-4 can induce adhesion molecules and promote lymphocyte proliferation. IL-13, mainly secreted by activated Th2, can promote the differentiation and proliferation of B cells, and is not conducive to the improvement of AR symptoms [29]. Therefore, reducing the inflammation level can significantly improve AR. In this study, the levels of inflammatory factors in Group B were lower than those in Group A after treatment, revealing that Jade Wind-Barrier Powder reduced the inflammatory reactions of the body and improved the clinical efficacy.

In conclusion, Jade Wind-Barrier Powder combined with Loratadine can improve the clinical symptoms, the body's immunity, inflammation levels and disease recurrence rate of PAR patients, exhibiting significant clinical efficacy. Although some achievements have been obtained in this study, the mechanism of drug action needs to be further explored.

Disclosure of conflict of interest

None.

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