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Airway function indicators and blood indicators in children with dust mite allergic rhinitis after sublingual immunotherapy

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ABSTRACT

Objective: To evaluate the airway function indicators and blood indicators in children with dust mite allergic rhinitis after sublingual immunotherapy. **Methods:** A total of 68 children with dust mite allergic rhinitis treated in our hospital from November, 2012 to October, 2015 were selected as the research subjects and randomly divided into observation group 34 cases and control group 34 cases. The control group received clinical routine therapy for allergic rhinitis, the observation group received sublingual immunotherapy, and then differences in basic lung function indicator values, small airway function indicator values and levels of serum inflammatory factors as well as serum ECP, TARC, Eotaxin-2 and VCAM were compared between two groups after treatment. **Results:** The FVC, FEV1, PEF and FEV1/FVC values of the observation group after treatment were higher than those of the control group (P<0.05); the MMEF, MEF50% and MEF25% values of the observation group were higher than those of the control group, and the proportion of AHR was lower than that of the control group (P<0.05); the serum IL-4, IL-9, IL-12, IL-13 and IL-16 levels of the observation group after treatment were lower than those of the control group, and the IL-10 and IL-12 levels are higher than those of the control group (P<0.05); the serum ECP, TARC, Eotaxin-2 and VCAM levels of the observation group children after treatment were lower than those of the control group (P<0.05). **Conclusions:** Sublingual immunotherapy for children with dust mite allergic rhinitis can optimize the airway function, reduce the systemic inflammatory response and eventually improve the children's overall state, and it's has positive clinical significance.

1. Introduction

Allergic rhinitis belongs to the chronic inflammation of nasal mucosa, it is common in clinical practice, and relevant statistics show that the incidence rate of allergic rhinitis is as high as 25% in preschool children[1,2]. Allergic rhinitis brings huge inconvenience to the normal life of children, is easily evolved to asthma with improper control, and causes permanent airway function and lung function damage. Dust mites are the main allergens of allergic rhinitis attack, and in addition to avoiding contact with allergens, the conventional methods for the treatment of allergic rhinitis include antihistamines, glucocorticoid, anti-leukotrienes, nasal decongestants, etc., but the effect only alleviates the illness and cannot radically reduce allergy attacks[3]. Immunotherapy is the most effective treatment for allergic rhinitis, which induces the immune tolerance and has the long-term effects. This research mainly evaluates the airway function indicators and blood indicators in children with dust mite allergic rhinitis after sublingual immunotherapy, now reported as follows:

2. Materials and methods

2.1. General information

A total of 68 children with dust mite allergic rhinitis treated in our hospital from November, 2012 to October, 2015 were selected as

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the research subjects, including 37 male cases and 31 female cases. Inclusion criteria were as follows: 1) the children were not in the acute phase and met the diagnostic criteria for allergic rhinitis; 2) prick test result of dust mites was positive before treatment, and that of other allergens was negative; 3) the children didn't receive dust mite extract treatment in the past; 4) the children were without immunodeficiency disorders; 5) the children didn't receive anti-allergy medication; 6) the children received intranasal corticosteroid treatment for more than 1 month but the effect was poor.

Included children were randomly divided into observation group (n=34) and the control group (n=34), control group included 20 male cases and 14 female cases, they were 2-11 years old, the average was (6.38±1.02) years, the course of disease was 1-5 years and the average was (2.17±0.28) years; observation group 18 male cases and 16 female cases, they were 2-10 years old, the average was (6.15±0.94) years, the course of disease was 1-6 years and the average was (2.09±0.41) years. There was no statistically significant difference in baseline data between the two groups (P>0.05) and they were comparable.

2.2. Treatment method

The control group received routine therapy for allergic rhinitis, including oral administration of antihistamines and corticosteroids as well as nasal drip of decongestants and anticholinergic drugs.

The observation group received sublingual immunotherapy, and the specific implementation was as follows: dust mite drops were dropped under the tongue of children with parents' help, administered for about 3 min and swallowed, and the daily administration time was fixed. Dust mite drops treatment was divided into dose-increasing period and dose-maintaining period, medication during increasing period included drops No. 1 (1 μg/mL), No. 2 (10 μg/mL) and No. 3 (100 μg/mL), the dose was 7 days per week and 1, 2, 3, 4, 6, 8 and 10 drops/day in turn, drops No. 4 (333 μg/mL) was applied from the 4th week, 3 drops/time, and the drip was continued for two years.

2.3. Observe indicators

Spirometer was used to measure basic lung function, including forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), highest expiratory flow (PEF), forced expiratory volume in the first second and forced vital capacity ratio (FEV1/FVC), *etc*., and they were in terms of the percentage of expected values. Indicators representing small airway function were measured at the same time, including the maximum mid-expiratory flow (MMEF), maximum expiratory flow when 50% of the FVC has been exhaled (MEF50%) and maximum expiratory flow when 25% of the FVC has been exhaled (MEF25%). Bronchial provocation test was carried out, positive meant FEV1 reduction 20% compared with basic value, namely high reactivity AHR.

Peripheral venous blood was drawn after treatment and centrifuged to get supernatant, and enzyme-linked immunosorbent was used to determinate the levels of the interleukin-4 (IL-4), interleukin-9 (IL-9), interleukin-10 (IL-10), interleukin-12 (IL-12), interleukin-13 (IL-13) and interleukin-16 (IL-16); eosinophil cationic protein (ECP), thymus activation regulated chemokine (TARC), eosinophil chemotactic factor-2 (Eotaxin-2), vascular cell adhesion molecule-1 (VCAM-1) levels were determinated.

2.4. Statistical methods

SPSS 23.0 software was used to statistically analyze the above data, measurement data (mean±sd) was analyzed by the t test, counting data was by *chi*-square test, and the results were judged as statistically significant different at a level of P<0.05.

3. Results

3.1. Basic lung function

After observation group receive sublingual immunotherapy, FVC, FEV1, PEF and FEV1/FVC values re higher than those of the control group (P<0.05), as shown in Table 1.

Table 1
Basic lung function index levels of two groups after treatment.

Groups	FVC (%)	FEV1 (%)	PEF (%)	FEV1/FVC
Observation group	93.15±3.06	90.23±7.32	81.23±5.39	85.36±4.32
Control group	72.34±5.03	70.56±6.52	67.17±4.76	71.53±5.88
χ^2	8.293	9.172	7.231	8.374
P	<0.05	<0.05	<0.05	<0.05

3.2. Small airway function

The results showed as follows: the MMEF, MEF50% and MEF25% values of the observation group are higher than those of the control group, and the proportion of AHR is lower than that of the control group (P<0.05), as shown in Table 2.

Table 2
Comparison of small airway function index values after different treatment (%).

Groups	MMEF (%)	MEF50 (%)	MEF25 (%)	AHR (%)
Observation group	84.27±4.34	78.65±6.02	72.49±4.39	2.49%
Control group	65.28±5.93	54.93±4.27	56.71±5.03	8.28%
χ^2	6.493	7.293	8.485	6.483
P	<0.05	<0.05	<0.05	<0.05

3.3. Serum inflammatory factor levels

The serum IL-4, IL-9, IL-12, IL-13 and IL-16 levels of the observation group after treatment are lower than those of the control group, and the IL-10 and IL-12 levels are higher than those of the control group (P<0.05), as shown in Table 3.

3.4. Serum ECP, TARC, Eotaxin–2 and VCAM level

Serum ECP, TARC, Eotaxin-2 and VCAM levels of the observation group children after treatment are lower than those of the control group (P<0.05), as shown in Table 4.

4. Discussion

Allergic rhinitis is a clinical common respiratory allergic disease, and children are high-risk group and mostly associated with allergic constitution. Studies have shown that there is obviously abnormal small airway function in allergic rhinitis patients when compared with normal people, indicating that all these patients have early airway changes that might develop into asthma[4,5]. Children with allergic rhinitis have to receive positive early intervention treatment so as to slow down or even reverse the outcome of airway damage and long-term progress to asthma. Breathing and airway function damage is the first performance of children with allergic rhinitis, and it is also the main macroeconomic index of the effectiveness of clinical intervention. FVC, FEV1, PEF and forced expiratory volume in FEV1/FVC are the main indicators currently used to measure lung function, and in cases of obviously abnormal lung function, the values of above indicators can be greatly reduced[6,7]. The research results show that FVC, FEV1, PEF and FEV1/FVC values of observation group of children after treatment are improved, which indicates at first that children with allergic rhinitis can be surely with lung function damage, and also shows that sublingual immunotherapy has excellent effect and can effectively improve children's impaired lung function.

Small airway belongs to artificial concept that refers to the airway with diameter of less than 2 mm, its resistance accounts for less than 20% of total airway resistance, and air flow is dominated by laminar flow. The maintenance of small airway structure is dependent on the elastic fiber of lung tissue, and damaged elastic fiber will cause narrowed and even closed small airway diameter. As the small airway wall is thin, inflammation can affect full-thickness airway and even the surrounding tissue, and the secretion and exudate can block the airway, settle and cause disease[8]. Above research detected the small airway function of patients after treatment, the results show that the MMEF, MEF50% and MEF25% values of observation group increase after the treatment and the proportion of AHR decreases. MMEF, MEF50% and MEF25% are important indicators measuring end airway function, and normal FEV1 value and decreased values of above indicators may be the early inflammatory changes of allergic diseases not associated with asthma[9,10] . In the study, test results of small airway function show that sublingual immunotherapy can early optimize small airway function in patients and avoid that inflammatory factors gradually erode small airway and eventually cause a serious lung function injury and asthma.

Patients with severe allergic rhinitis can be with systemic reaction, mainly involving a variety of cytokines and inflammatory mediators. IL-10 is produced by activated mononuclear cells and epithelial cells, it has wide inflammation-inhibiting effect, it can effectively inhibit Th0, Th1 and Th2 cell proliferation and activation and inhibit mast cell secretion and IgE production, and it plays an important role in the pathological process in type Ⅰ allergic diseases. IL-12 can induce $CD4^+$Th cell differentiation into Th1 cells, inhibit Th2 cell generation, participates in specific IgE synthesis and inhibit mast cell degranulation, and therefore it plays a regulating role in allergic rhinitis in each link[11]. IL-13 is mainly secreted by activated $CD4^+$Th2 cells, and by inducing B cell proliferation and differentiation, it can promote the synthesis and secretion of IgE and induce airway hyperresponsiveness. IL-16 is synthesized by a variety of cells, which belongs to pro-inflammatory cytokines, is produced

Table 3
Comparison of serum inflammatory factor levels after received different treatment (ng/L).

Groups	IL-4	IL-9	IL-10	IL-12	IL-13	IL-16
Observation group	21.04±1.76	37.54±2.93	17.23±1.34	271.29±23.65	162.92±13.18	78.23±5.47
Control group	57.29±4.81	79.63±6.11	12.18±1.05	198.62±17.44	321.05±25.95	129.61±11.83
t	8.232	9.823	5.384	8.293	9.235	8.294
P	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05

Table 4
Comparison of serum ECP, TARC, Eotaxin-2 and VCAM levels between two groups after treatment.

Groups	ECP (μg/L)	TARC (pg/mL)	Eotaxin-2 (pg/Ml)	VCAM (μg/L)
Observation group	16.23±1.41	0.27±0.02	1.92±0.15	452.93±39.55
Control group	25.95±2.37	0.48±0.03	3.05±0.27	673.05±59.88
t	7.293	6.934	7.034	9.172
P	<0.05	<0.05	<0.05	<0.05

in the early type Ⅰ allergy, can induce T lymphocyte, eosinophil and macrophage chemotaxis and activation and is an important factor of local inflammatory reaction. IL-4 is the most important regulatory factor of IgE synthesis process, it belongs to the IgE-specific inducer and mast cell growth factor, and it can promote the humoral immune response. IL-9 plays an important role in asthma attack, it can induce mast cell grow and T cell proliferation, and it can work together with IL-4 and inhibit IL-2 function [12]. The study above detected the serum inflammatory cytokine levels of the two groups, and the result shows: serum IL-4, IL-9, IL-12, IL-13 and IL-16 levels of the observation group after treatment are reduced, and IL-10 and IL-12 levels are increased, indicating that after sublingual immunotherapy, systemic inflammatory response of the children is reduced, anti-inflammation ability is enhanced.

Eosinophil infiltration and nasal mucosal chronic inflammation are important characteristics of allergic rhinitis, eosinophils are considered to play a role in allergic rhinitis through the release of toxic protein[13]. ECP is toxic protein released by activated acidophilic granulocyte, and its level directly represents the severity of patients with allergic rhinitis. Both TARC and eosinophil chemotactic factor-2 (Eotaxin-2) have the effect of inducing specific human T cell chemotaxis, TARC is expressed in thymus and Eotaxin-2 is expressed in peripheral blood mononuclear cells. Studies suggest that TARC and Eotaxin-2 of patients with allergic rhinitis are highly expressed in CCR3 receptor, indicating that they promote eosinophils arrival at inflammatory part and cause related clinical symptoms through CCR3 receptor signal transduction pathway. VCAM-1 is an important cell adhesion molecule can be combined with eosinophils surface ligand and lead to eosinophil migration and participate in the occurrence of allergy[14,15]. This study compares levels of the above indexes after treatment, and results show that the serum ECP, TARC, Eotaxin-2 and VCAM levels of the observation group patients after treatment reduce, indicating that specific immunotherapy can reduce eosinophil activity and inhibit allergic reaction in children.

To sum up, it can be concluded as follows: sublingual immunotherapy for children with dust mite allergic rhinitis can optimize the airway function, reduce the systemic inflammatory response and eventually improve the children's overall state, and it's worth popularization in clinical practice in the future.

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