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Effect of budesonide and cetirizine hydrochloride on neurotrophic factor, airway function and chemokines CCL17 and CCL22 in patients with allergic rhinitis

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ABSTRACT

Objective: To investigate the effect of budesonide combined with cetirizine hydrochloride on neurotrophic factor, airway function and chemokines CCL17 and CCL12 in patients with allergic rhinitis. **Methods:** A total of 123 patients with Allergic Rhinitis were randomly divided into three groups, A group treated with budesonide nasal spray, B group treated with cetirizine hydrochloride, C group treated with budesonide combined with cetirizine hydrochloride, then the Neurotrophic factors, airway function indexes and chemokines CCL17 and CCL12 levels in three groups were compared. **Results:** Before the treatments, the three groups of patients in neurotrophic factor, airway function index and chemokines CCL17, CCL22 have no differences, Compared with before the treatments, after receiving different treatments, the three groups of patients in all indicators were Showed significant differences. In the indexes of neurotrophic factor (NGF, BDNF, NT-3mRNA expression), there was no significant difference between group A and group B, and group C was lower than group A and B. In airway function indexes (FVC, FEV1 and PEF), A group was significantly higher than B group, C group was significantly higher than A group; In the chemokines CCL17 and CCL22 indicators, C group was lower than A group, A group was lower than B group, the difference was significant. **Conclusions:** Budesonide combined with cetirizine hydrochloride in the treatment of Allergic Rhinitis, can effectively control the patients' neurotrophic factor, pulmonary ventilation and chemokine CC17, CCL22 indicators, the effect is better than Budesonide alone or Cetirizine hydrochloride.

1. Introduction

Variant rhinitis (AR) is generally mediated by immunoglobulin E (IgE), releasing histamine based inflammatory mediators, and other immune active cells and cytokines, which are associated with chronic inflammatory diseases of the nasal mucosa，it is a common allergic disease in clinical otorhinolaryngology Department whose symptoms manifested as sneezing, runny nose, itchy nose[1]. AR is a multifactorial disease, and the predisposing factors are complex. Atopy, sensitization, individual mental state, living habits, external environment and other factors are related to the variability of rhinitis. With the rapid development of China's economy and the transformation of social industrial structure, people's lifestyle has also undergone tremendous changes. While creating material satisfaction, the industrial society also brings negative impacts such as environmental pollution aggravating, life rhythm speeding up and social pressure increasing, and the continuous aggravation of air pollution is closely related to the increasing incidence of AR[2−5]. As a common clinical disease, Variant rhinitis does not pose a threat to the lives of patients, but it seriously affects the quality of life of patients, when it develops to a certain extent, it can also induce other respiratory diseases, such as otitis media, asthma, respiratory tract infection, chronic sinusitis, etc[6]. Therefore, the use of efficient and safe treatment program for patients with strain rhinitis is of great significance. In this study, budesonide combined with cetirizine hydrochloride was used to treat patients with strain rhinitis,the analysis report is as follows.

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2. Informations and methods

2.1. General information

A total of 123 patients with allergic rhinitis treated in our hospital from June 2016 to June 2017 were selected as the research objects. The age ranged from 16-68 years, with an average age of 33.1 years, and the course of disease was (6.2 ± 2.8) years. Among them, 59 cases were male and 64 cases were female. 123 patients were in line with the 2009 Wuyishan meeting guidelines for the diagnosis and treatment of adult allergic rhinitis, and in recent months did not receive tranquilizers, antihistamines, corticosteroids and immunosuppressive drugs and other related treatment, with no asthma related disease history, and has no allergic reaction to the drug. After obtaining the informed consent of all patients, all patients were randomly divided into three groups, 40 patients in group A, including 20 males and 20 females, who received budesonide spray (AstraZeneca, J20140047); 40 patients in group B, including 21 males and 19 females, who received Cetirizine Hydrochloride Tablets (Suzhou Pharmaceutical Company Limited, Zhunzi H19980014); 43 patients in group C, including 18 males and 25 females, who received budesonide nasal spray combined with Cetirizine Hydrochloride Tablets. There was no significant difference between the three groups in age, gender, course of disease and general information (P>0.05), which was comparable.

2.2 Treatment methods

Group A received budesonide spray treatment,Medication once in the morning and evening with a single dose of 0.5 μg (1 each nostril spray), received continuous treatment for 14 d; Patients in group B received Cetirizine Hydrochloride Tablets, 1 time a night, with a single dose of 10 mg per time, and received continuous treatment for 14 d; Patients in group C were treated with budesonide spray combined with Cetirizine Hydrochloride Tablets, Budesonide aerosol medication 1 time in the morning and evening with a single dose of 0.5 μg (1 each nostril spray), at the same time, take 10 mg Cetirizine Hydrochloride Tablets once every night, and receive continuous treatment for 14 d.

2.3 Observation indexes

2.3.1 The levels of neurotrophic factors (nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophic protein-3 (NT-3) mRNA) were detected by real-time quantitative RT-PCR[7,8] in three groups before and after treatment.

2.3.2 The pulmonary ventilation function of patients before and after treatment was measured by the BTL-08SPIRO pulmonary function test instrument. All patients completed no less than 3 tests, and The final evaluation results obtained the best results (variation rate <5%).

2.3.3 The levels of human thymus and activation-regulated chemokine (TARC) CCL17 and macrophage-derived chemokine (MDC) CCL22 in peripheral blood of patients before and after treatment were detected by enzyme linked immunosorbent assay[9-11].

2.4 Statistical analysis

The data were analyzed by SPSS 15.0 statistical software, Statistical analysis was carried out by (means ± standard deviation), and the t test was used. The enumeration data was checked by chi square test. P<0.05 indicated that the two groups had statistically significant differences.

3. Results

3.1 Comparison of neurotrophic factors (nerve growth factor (NGF), brain-derived neurotrophic factor (BDNF), neurotrophic protein-3 (NT-3) mRNA) among three groups

The expression levels of NGF, BDNF and NT-3 mRNA were compared among the three groups,the results showed that: Before the experiment, there was no significant difference among the three groups (P>0.05); After receiving different drug treatments, compared with before treatment, each index were significantly changed in the three groups (P<0.05). After treatment, there was no significant difference between A group and B group in each index (P>0.05); there were significant differences in NGF, BDNF and NT-3 between C group and A group, C group and B group, and there was statistical significance (P<0.05). Details are shown in Table 1.

Table 1.

Comparison of NGF, BDNF and NT-3mRNA levels among the three groups.

Group	n	Detection time	NGF (ng/g)	BDNF (ng/L)	NT-3 (pg/mL)
A	40	Before treatment	6.42 ± 1.72	79.62 ± 16.84	54.79 ± 10.29
		After treatment	4.56 ± 1.48*	36.28 ± 11.62*	22.58 ± 4.02*
B	40	Before treatment	6.77 ± 1.83	77.93 ± 18.21	55.20 ± 9.89
		After treatment	4.53 ± 1.53*	37.31 ± 12.02*	21.82 ± 3.86*
C	43	Before treatment	6.21 ± 1.54	78.37 ± 17.35	55.61 ± 9.48
		After treatment	3.22 ± 1.03*&#	27.82 ± 9.17*&#	17.33 ± 2.73*&#

Note: compared with before treatment, *P<0.05; compared with group A, &P<0.05; compared with group B, #P<0.05.

Table 2.

Comparison of FVC, FEV1 and PEF indexes among the three groups.

Group	*n*	Detection time	FVC (L)	FEV1 (L)	PEF (L/min)	FEV1/FVC (%)
A	40	Before treatment	3.61 ± 0.57	2.21 ± 0.72	53.33 ± 6.82	53.33 ± 6.82
		After treatment	4.93 ± 0.38$^{*\#}$	2.96 ± 0.52$^{*\#}$	67.02 ± 7.51$^{*\#}$	65.28 ± 5.30$^{*\#}$
B	40	Before treatment	3.70 ± 0.75	2.12 ± 0.64	52.72 ± 7.60	55.62 ± 7.15
		After treatment	4.48 ± 0.42*	2.58 ± 0.59*	62.35 ± 7.82*	57.12 ± 5.33*
C	43	Before treatment	3.82 ± 0.51	2.61 ± 0.58	54.03 ± 7.12	54.56 ± 6.61
		After treatment	5.42 ± 0.62$^{*\&\#}$	3.25 ± 0.53$^{*\&\#}$	73.37 ± 8.34$^{*\&\#}$	70.13 ± 5.06$^{*\&\#}$

Note: compared with before treatment, $^{*}P$<0.05; compared with group A, $^{\&}P$<0.05; compared with group B, $^{\#}P$<0.05.

Table 3.

Comparison of chemokine CCL17 and CCL22 indexes among the three groups.

Chemotactic factor	Detection time	Group A (*n*=40)	Group B (*n*=40)	Group C (*n*=43)
CCL17	Before treatment	670.03 ± 42.19	669.33 ± 41.41	671.52 ± 39.71
	After treatment	614.21 ± 22.24$^{*\#}$	630.29 ± 21.17*	605.01 ± 11.47$^{*\&\#}$
CCL22	Before treatment	818.55 ±51.27	820.81 ± 50.12	819.73 ± 49.95
	After treatment	720.03 ± 26.48$^{*\#}$	769.72 ± 25.68*	704.12 ± 21.62$^{*\&\#}$

Note: compared with before treatment, $^{*}P$<0.05; compared with group A, $^{\&}P$<0.05; compared with group B, $^{\#}P$<0.05.

3.2 Comparison of FVC, FEV1 and PEF indexes among the three groups

The pulmonary ventilation function of the three groups was measured and compared. Before the experiment, there was no significant difference in FVC, FEV1 and PEF indexes between the three groups, and there was no statistical significance (P>0.05); After receiving different drug treatment, compared with before treatment, there were statistically significant differences among the three groups′ FVC, FEV1 and PEF indicators (P<0.05); Details are shown in Table 2.

3.3 Comparison of chemokine CCL17 and CCL22 indexes among the three groups

Before the experiment, there was no significant difference in the chemokines CCL17 and CCL22 among the three groups (P>0.05); After the treatment of different drugs, the data of three groups were analyzed by one-way ANOVA. The results showed that there were significant differences among the three groups in the content of chemokines CCL17 and CCL22, with statistical significance (P>0.05); Levene homogeneity test was used to further analyze the differences between groups,the results shows that the variance of A, B and C in the three groups was homogenesis, however, the difference is not homogeneous over the chemokine CCL22 index, Therefore, the LSD test and Tamhane`s T2 test were used to analyze the data. The results showed that there were significant differences in the levels of CCL17 and CCL22 between the A group and the B group after the drug treatment, and the difference was statistically significant (P>0.05); There were significant differences between group C and group A and group B, with statistical significance (P<0.05). Details are shown in Table 3.

4. Discussion

Allergic rhinitis is one of the common diseases in otorhinolaryngology, which can be divided into three types: mild, moderate and severe according to the different course of disease. The characteristic of the lesion is that the allergen is combined with immunoglobulin E on platelets and eosinophils after entering the patient,thus promoting the release of the cell medium[12,13]. At the same time, the transmission of antigen peptide signals increases the number of Th2 helper cells and increases the function, while the number of Th1 helper cells decreases in reverse, which leads to immune dysfunction. The external clinical symptoms are nasal congestion, nasal itching, sneezing and so on[14–16]. The pathological changes are generally manifested as telangiectasia and vascular permeability enhancement. The secretion of histamine increases histamine levels, eosinophils infiltration, and then cause inflammatory changes in the nasal cavity[17].

At present, antihistamines and glucocorticoids are the primary choice for the treatment of AR[18]. Budesonide, a common nasal spray, is a glucocorticoid with high local anti-inflammatory effect, It can increase the effective promotion of the lysosomal membrane, endothelial cells and smooth muscle cells of stability, reduce the immune response and antibody production, and decrease the level of histamine, ease of enzymatic processes, reduce the content of shrinkage material so as to realize the clinical effect of bronchial smooth muscle contraction to reduce reaction. By spraying drugs, it can direct lesions, can immediately play a pharmacodynamics, so it has good practice effect. Cetirizine, one of the second generation antihistamines, has potent anti-inflammatory effects. It can rapidly bind to histamine H1 receptors on target cell membranes after administration, thereby blocking histamine activation of target cells. In addition to the potent anti-inflammatory effect, cetirizine has the advantage of combination therapy because of its metabolism that does not pass through the liver.

In recent years, through the study of neuropeptides, we found that

neurotrophic factors not only maintain the survival and growth of neurons, there is also a certain correlation between neural regulation and the pathogenesis of AR, Neurotrophic factors can trigger airway hyperresponsiveness by stimulating airway nerve cells, and may also participate in airway remodeling[19,20]. Nerve growth factor (NGF), as a neuropeptide inducer, can promote the secretion of neuropeptides and play an important role in the pathogenesis of AR. Studies have shown that brain derived neurotrophic factor (BDNF) can selectively enhance the antigen-specific immunoglobulin E without affecting IgA or IgG4, and reduce the apoptosis of eosinophils. The expression of neurotrophic protein-3 (NT-3) mRNA is linearly related to AR, which can be used as a molecular biological marker for evaluating the condition of the disease. Due to the inflammatory response of nasal mucosa, AR patients may have some influence on the lower respiratory tract, which leads to certain changes in pulmonary function. Studies have shown that allergic rhinitis can cause inflammation of the bronchial mucosa, leading to the decline of FEV1, and even lead to lower airway remodeling. Therefore, if not treated in time,If the pulmonary ventilation function is not improved, with the development of the disease course, it may cause asthma and other diseases. Chemokines CCL17 can enhance the hyperresponsiveness of the upper respiratory tract, induce eosinophils, and play a role in the formation and development of airway inflammation. Chemotactic factor CCL22 can induce eosinophils, which are important chemokines in allergic rhinitis and participate in the pathogenesis of AR.

In recent years, the results of related studies have shown that budesonide alone or other antihistamines can achieve certain efficacy in the treatment of AR[22,23]. In this study, budesonide and cetirizine were combined with topical and systemic anti allergic reactions, the results showed that all the indexes were better than single drug use, and the combination of drugs played a complementary role, thereby improving the curative effect.

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