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Original Article

Inhaled corticosteroids combined with spleen aminopeptide for treatment of children with allergic rhinits and asthma syndrome

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Abstract: Objective: To explore the clinical efficacy of corticosteroids administrated by nasal inhalation and spleen aminopeptide (SA) in the treatment of children with combined allergic rhinits and asthma syndrome (CARAS). Methods: A total of 80 children diagnosed with CARAS treated from February 2016 to February 2017 were randomly divided into treatment group (n=40) and control group (n=40). Among them, the children in the treatment group received inhaled corticosteroids (ICS) combined with SA, and those in the control group only ICS without an oral administration of SA. The total clinical effective rate, the disappearing time of the patient's signs and symptoms and the immunological examination results were compared between the two groups of patients. Results: The total effective rate in the treatment group was 90.00%, while that in the control group was 52.50% (P<0.001). The disappearing time of fever, cough, swelling of tonsil and pulmonary rales of the children in the treatment group were shorter than that of the children in the control group, with significantly statistical difference (all P<0.01). The levels of T-lymphocyte subsets (including CD_3^+ CD_4 regulatory cells, CD_3^+ CD_8 regulatory cells and the ratio of CD_4/CD_8) of the children in the treatment group were higher than those of the children in the control group after treatment. The differences were statistically significant (P<0.001). Conclusion: The application of corticosteroids by nasal inhalation combined with SA as early as possible has a better efficacy than ICS alone in the treatment of children with CARAS.

Keywords: Children with combined allergic rhinitis and asthma syndrome, inhaled corticosteroids, spleen aminopeptide

Introduction

Combined allergic rhinits and asthma syndrome (CARAS) refers to clinical or subclinical allergy symptoms in the upper respiratory tract (allergic rhinitis) and the lower respiratory tract (asthma) that commonly occur at the same time. Immature immune system and immune dysfunction in children are the main causes of CARAS [1, 2]. At present, glucocorticoid and spleen aminopeptide (a new immunomodulator) extracted from fresh pig spleen are mainly used clinically for the treatment of autoimmune disorders, immune deficiency and cellular immune dysfunction [3, 4]. In recent years, some experts pointed out that the joint diagnosis and treatment of children with CARAS is conducive to improving the diagnostic accuracy of the two diseases and reducing the repeated use of drugs, thus decreasing the rate of misdiagnosis and improving the clinical efficacy. Joint diagnosis and treatment is clinically practical, which has been promoted and applied currently. As the use of glucocorticoid alone has poor efficacy, and the efficacy of traditional Chinese medicine is unknown, the clinical efficacy of nasal inhalation of corticosteroids combined with spleen aminopeptide (SA) in the treatment of children with CARAS was investigated in this study to obtain more evidence-based medical basis for new combined therapy.

Materials and methods

General data

A total of 80 children diagnosed with CARAS who were treated in Xingtai People's Hospital

Affiliated to Hebei Medical University from February 2016 to February 2017 were selected.

Inclusion criteria: Firstly, patients with a typical history of familial asthma or an allergy history; secondly, patients with sudden and recurrent allergic symptoms in upper or lower respiratory tract (including nasal itching, sneezing, stuffy nose and runny nose); thirdly, patients diagnosed with mild or moderate symptoms of acute exacerbation of bronchial asthma through auxiliary examinations [5].

They were divided into treatment group (n=40) and control group (n=40) according to the method of random number table. Among them, the children in the treatment group received inhaled corticosteroids (ICS) combined with SA, and those in the control group only ICS without an oral administration of SA.

Exclusion criteria: Firstly, patients with severe asthma; secondly, patients whose wheezing and coughing were caused by tumors or mycobacterium tuberculosis; thirdly, patients whose nasal ventilation dysfunction was caused by nasal septum deviation, nasal polyps, etc.; fourthly, patients with congenital heart disease, serious diseases of heart, liver, kidney or other major organs or blood system diseases [6].

Patients who have received other treatments in addition to hormones in the past were enrolled in this study after drug withdrawal for 2 weeks.

The study protocol was approved by the Ethics Committee of Xingtai People's Hospital Affiliated to Hebei Medical University, and the informed consent was obtained from parents of the patients.

The 80 patients included 43 males aged 3-9 years old and 37 females aged 4-10 years old. They were randomly divided into treatment group (n=40) and control group (n=40).

Treatment methods

Patients in the treatment group were given corticosteroids (budesonide aerosol, administrated by aerosol inhalation with a driven atomizer, 200 μg/time, twice/day) in the acute phase on the basis of anti-inflammatory symptomatic treatment, and spleen aminopeptide oral lyophilized powder (Dalian Baili Tianhua Pharmaceutical Co. Ltd., 2 mg/time, once every other day, dissolved in cold water for oral administration before sleep with one month as a treatment course) as well as anti-inflammatory and anti-viral treatments in the remission phase. The patients paid attention to keep warm, carry out daily care and maintain a reasonable diet in the remission phase. Those in the control group were also given corticosteroids (budesonide aerosol, administrated by aerosol inhalation with a driven atomizer, 200 μg/time, twice/day) in the acute phase, but they did not receive oral administration of SA lyophilized powder. Other treatments were the same as what has been conducted in the treatment group.

Observation indicators

Total effective rate after treatment, the disappearing time of symptoms and signs of CARAS and the levels of T-lymphocyte subsets (including CD_3^+ CD_4 regulatory cells, CD_3^+ CD_8 regulatory cells and the ratio of CD_4/CD_8) after treatment were compared between the two groups of patients [7, 8]. All the patients with CARAS received one treatment course (one month). The aforementioned indicators were observed after treatment. In order to see the long-term efficacy, a follow-up was conducted for 6 months. The clinical efficacy was assessed according to the following criteria: ineffective, the duration and the number of attacks were not reduced obviously; effective, the number of clinical seizures was reduced obviously after drug withdrawal, the disease attacked once to twice, and the duration of the disease was shortened; significantly effective, after a course of treatment, respiratory tract infection was not observed again within 6 months after drug withdrawal [9]. Total effective rate = significantly effective rate + effective rate.

Statistical treatment

Statistical Product and Service Solutions 18.0 software was adopted. The measurement data were expressed as mean ± standard deviation ($\bar{x} \pm sd$) using two independent samples t-test, and the enumeration data were expressed as percentage using χ^2 test. $P<0.05$ suggested that there was statistical difference, and $P<0.001$ indicated the difference was statistically significant.

Table 1. Comparison of general information between the two groups of patients

Group	Case	Male/Female	Age (years old)	Infection (Year/Times)
Treatment group	40	21/19	3.20±0.45	7.2±2.1
Control group	40	22/18	3.20±0.27	7.6±2.3
Statistical value		0.000	0.000	0.812
P		1.000	1.000	0.419

Table 2. Comparison of clinical efficacy between the two groups of patients (n, %)

Group	Case	Significantly effective	Effective	Ineffective	Total effective rate
Treatment group	40	24 (60.00)	12 (30.00)	4 (10.00)	36 (90.00)
Control group	40	10 (25.00)	11 (27.50)	19 (47.50)	21 (52.50)

Note: χ^2=15.591, P<0.001.

Table 3. Comparison of the disappearing time of symptoms and signs between the two groups of patients (hour)

Group	Case	Fever	Cough	Swelling of tonsil	Pulmonary rales
Treatment group	40	2.1±1.2	4.5±1.2	3.2±1.2	5.2±1.4
Control group	40	3.4±0.8	5.2±1.2	4.1±1.2	6.2±1.2
t		5.701	3.456	3.354	4.116
P		<0.001	<0.001	0.001	<0.001

Table 4. Comparison of immunological examination results between the two groups of patients (%)

Group	Case	CD_3^+ CD_4	CD_3^+ CD_8	CD_4/CD_8
Treatment group	40	36.68±4.56	25.95±5.48	1.63±0.41
Control group	40	30.16±5.68	21.16±4.26	1.13±0.52
t		-5.661	-4.365	-4.775
P		<0.001	<0.001	<0.001

Results

Comparison of basic information between the two groups of patients

There were 21 males and 19 females in the treatment group with an average age of 3.20±0.45 years old and an annual recurrent infection of 7.2±2.1 times, and the patients in the control group included 22 males and 18 females with an average age of 3.20±0.27 years old and an annual recurrent infection of 7.6±2.3 times. There were no statistical significances between the two groups of patients in terms of gender, age, infection (P>0.05). The information was comparable (**Table 1**).

Observation of clinical efficacy in the two groups of patients

It was found that among the 40 patients in the treatment group, 36 patients' clinical seizures were reduced obviously after drug withdrawal, the disease attacked once to twice, and the duration of the disease was shortened The total effective rate in the treatment group was 90.00%, while that in the control group was 52.50% (P<0.001, **Table 2**). The disappearing time of fever, cough, swelling of tonsil and pulmonary rales of the children in the treatment group was shorter than that of the children in the control group, with obviously statistical significance (P<0.001, P<0.001, P=0.001, P<0.001, respectively). See **Table 3**. The levels of T-lymphocyte subsets (including CD_3^+ CD_4 regulatory cells, CD_3^+ CD_8 regulatory cells and the ratio of CD_4/CD_8) of the children in the treatment group were higher than those of the children in the control group after treatment. The differences were statistically significant (P<0.001). See **Table 4**.

The clinical efficacy in the two groups of patients who received ICS combined with SA and ICS alone without oral administration of SA were observed (**Table 2**). The total effective rate in the treatment group was 90.00%, while that in the control group was 52.50% (χ^2= 15.591, P<0.001). The difference was statistically significant.

Comparison of the disappearing time of symptoms and signs between the two groups of patients

The disappearing time of fever, cough, swelling of tonsil and pulmonary rales of the patients in the treatment group was significantly shorter

than that of the patients in the control group. The difference showed significantly statistical significance (P<0.001). See **Table 3**.

Comparison of immunological examination results between the two groups of patients

After treatment, the levels of T-lymphocyte subsets (including CD_3^+ CD_4 regulatory cells, CD_3^+ CD8 regulatory cells and the ratio of CD_4/CD_8) of the children in the treatment group were higher than those of the children in the control group. The differences were very statistically significant (P<0.001, **Table 4**).

Discussion

In recent years, with an in-depth understanding of the pathogenesis of CARAS in children, it is known that the pathophysiological mechanism has been transformed from the past pure airway smooth muscle spasm theory to upper and lower airway inflammation theory [10]. From the anatomical point of view, the continuity of the nasal cavity and bronchus in the anatomical structure and physiological functions determines the close relationship between allergic rhinitis and asthma. In previous clinical practice, the treatment method of simple relief of bronchospasm and excessive dependence on bronchodilators has certain one-sidedness. The prevention of CARAS in children should focus on the elimination of the allergic reaction in the entire respiratory tract, thereby reducing the nasal and lower airway hyperresponsiveness. However, most of current treatment methods can only control the symptoms, but fail to cure rhinitis and asthma. As allergens cannot be avoided completely after drug withdrawal, the inflammatory response in the respiratory tract can be aggravated by repeated exposure to allergens, the clinical symptoms may occur repeatedly, and the disease can extend into adulthood, which finally develops into irreversible lung dysfunction. Nasal inhalation of glucocorticoids is currently known to be the best anti-inflammatory drug for the airway [11]. Avoiding allergen irritation is a key factor affecting the clinical outcome. When drug treatment is adopted, it is necessary to adjust the treatment protocol anytime according to the patient's condition.

SA is a new immunomodulator, which is mainly composed of peptides and nucleotides, extracted from fresh spleen of pigs and widely used in clinical treatment of autoimmune disorders, immunodeficiency and cellular immune dysfunction [12, 13]. Clinical studies have shown that spleen aminopeptide can improve cellular immune function, produce and release interferon and lymphokines. It can regulate the function of helper T cells to obviously increase the secretion amount of y-interferon, interleukin-6 and interleukin-2, enhance the activity of the mononuclear phagocytic system, improve the level of immunity in children with recurrent respiratory tract infection, and play a role in inhibiting the replication of virus in the body [14]. Some scholars have found in their studies that the application of spleen aminopeptide can significantly improve the number of T lymphocytes in the children, and obviously lower the incidence of recurrent respiratory tract infections in children without causing significant adverse reactions [15]. In this study, it was found that the total effective rate in the treatment group who received aerosol inhalation of glucocorticoids combined with oral administration of spleen aminopeptide was 90.00%, while that in the control group was 52.50%. The disappearing time of fever, cough, swelling of tonsil and pulmonary rales of the children in the treatment group was significantly shorter than that of the children in the control group, with significantly statistical difference (all P<0.01). After treatment, the levels of T-lymphocyte subsets (including CD_3^+ CD_4 regulatory cells, CD_3^+ CD_8 regulatory cells and the ratio of CD_4/CD_8) of the children in the treatment group were higher than those of the children in the control group, with significantly statistical difference (all P<0.001). All of these results suggested that spleen aminopeptide can improve the therapeutic effect by regulating the immune response, which is identical with the result reported in previous study of Chen et al. that the application of spleen aminopeptide can significantly improve the number of T lymphocytes in children as well as that reported in the study of he et al. that spleen aminopeptide can regulate relevant factors to relieve symptoms of bronchial asthma [16, 17].

However, in this study, it was required for patients who did not receive the treatment for the first time and have received other treatments in the past to stop drug administration for at least 2 weeks. Meanwhile, the compari-

son of clinical efficacy between the two groups would be influenced by the dose of the drugs, the temperature and the change in the weather which should be strictly controlled [18, 19].

This study showed that, compared with conventional treatment, the inhalation of glucocorticoids combined with spleen aminopeptide can obviously shorten the disappearing time of fever, swelling of tonsil and pulmonary rales and improve total effective rate in the treatment of children with recurrent respiratory tract infection [20]. Therefore, the inhalation of glucocorticoids combined with spleen aminopeptide is effective to enhance body immunity in the treatment of children with recurrent respiratory tract infection. Meanwhile, the children have good compliance during treatment. Thus, it is a safe and effective treatment method, which is worthy of clinical application.

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Disclosure of conflict of interest

None.

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