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Clinical Therapeutic Effects of Clarityne Combined with Singulair On Cough Variant Asthma in Children and Influence on Eosinophils in Sputum

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Abstract

Objective: To assess the clinical therapeutic effects of Clarityne combined with Singulair on cough variant asthma in children and the influence on eosinophils in sputum.

Methods: Seventy children with cough variant asthma admitted to our hospital from January 2018 to December 2019 were randomly divided into two groups (n=35) using a random number table. Control group was treated with Clarityne, while observation group was treated with Clarityne + Singulair. The clinical efficacy, disappearance time of symptoms and signs, serum inflammatory factors, eosinophils, immunoglobulins, pulmonary ventilation function indices and incidence rate of adverse reactions were compared.

Results: The total clinical effective rate was higher in observation group than that in control group (97.14% *vs.* 82.86%, P<0.05). The disappearance time of symptoms such as cough and wheezing was shorter in observation group than that in control group (P<0.05), and the disappearance time of pulmonary wheezing sound was shorter in observation group than that in control group (P<0.05). The levels of interleukin-2 (IL-2), IL-4 and C-reactive protein declined in both groups after treatment in comparison with those before treatment, and they were lower in observation group than those in control group after treatment (P<0.05). The concentrations of eosinophils in sputum and serum dropped in both groups after treatment in contrast with those before treatment (P<0.05), and they were lower in observation group than those in control group after treatment (P<0.05). In comparison with those before treatment, the levels of Immunoglobulin G (IgG), IgA and IgM rose in both groups after treatment, and they were higher in observation group than those in control group (P<0.05). Compared with those before treatment, the forced expiratory volume in one second (FEV1) and FEV1/forced vital capacity increased in both groups after treatment, and they were higher in observation group than those in control group (P<0.05). There was no significant difference in the incidence rate of adverse reactions between observation group and control group (5.71% *vs.* 2.86%, P>0.05).

Conclusion: Clarityne combined with Singulair has good efficacy in the treatment of cough variant asthma in children. It can effectively relieve the symptoms and signs of children, reduce their inflammatory response, regulate their immune function, and help improve their pulmonary ventilation function. The combination of the two drugs leads to few adverse reactions, which is safe and reliable.

Keywords: cough variant asthma; Clarityne; Singulair; eosinophils

INTRODUCTION

Cough variant asthma is a special type of asthma with chronic cough as the major manifestation, which occurs mostly in children. Children with cough variant asthma often exhibit symptoms such as wheezing and coughing, which seriously harm their physical and mental health [1,2]. Cough variant asthma in children is mainly treated by drugs, such as Clarityne (loratadine) and Singulair (montelukast sodium), both of which can be used in the treatment of asthma. To investigate the therapeutic effects of Clarityne combined with Singulair on cough variant asthma in children, 70 eligible cases treated in our hospital from January 2018 to December 2019 were selected and divided into two groups for a randomized controlled study.

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MATERIAL AND METHODS

Baseline clinical data

A total of 70 children with cough variant asthma who were admitted to our hospital from January 2018 to December 2019 were selected as subjects and randomly divided into two groups (n=35) using a random number table. In control group, there were 18 males and 17 females, aged 6-12 years old, with an average of (9.04 ± 2.33) years old. In observation group, there were 19 males and 16 females, aged 6-12 years old, with an average age of (8.92 ± 2.45) years old. No statistically significant differences were observed in the general data between the two groups (P>0.05), which were comparable. This study was approved by the hospital's Medical Ethics Committee.

Inclusion criteria: (1) Children diagnosed as cough variant asthma by clinical symptom observation, imaging examination and laboratory examination, (2) those with an age <14 years old, and (3) those whose parents were informed of the treatment plan and signed the informed consent.

Exclusion criteria: (1) Children with a history of Clarityne or Singulair allergy, (2) those complicated with other respiratory diseases, or (3) those complicated with systemic infection or autoimmune diseases.

Methods

Children in control group were treated with oral Clarityne (generic name: loratadine, manufacturer: Shanghai Schering-Plough Pharmaceutical Co. Ltd., approval No. NMPN H10970410, specification: 10 mg) at 10 mg/time, once daily. Children in observation group were treated with Clarityne + Singulair (generic name: montelukast sodium, imported from Merck Sharp & Dohme (Australia) Pty Ltd., registration No.H20120366, specification: 5 mg). The administration of Clarityne was the same as that in control group, and Singulair was taken orally at 5 mg/time, once daily. Both groups of patients were treated for 2 consecutive weeks.

Observation indices

The following items were compared between the two groups: (1) Clinical efficacy evaluated through the total effective rate: Total effective rate = (cured cases + improved cases)/total cases × 100%. The specific evaluation criteria were as follows: (A) Cured: Complete disappearance of symptoms such as cough and wheezing, no wheezing sound in lung auscultation, and no need of drug control. (B) Improved: Symptoms such as cough and wheezing were relieved and pulmonary wheezing sound was alleviated, with occasional asthma attacks that needed to be controlled by drugs. (C) Ineffective: Symptoms such as cough and wheezing were not alleviated and pulmonary wheezing sound was not relieved, with frequent asthma attacks that needed to be controlled by drugs [3]. (2) Disappearance time of symptoms and signs including cough and wheezing (symptoms), and pulmonary wheezing sound (sign). (3) Serum inflammatory factors including interleukin-2 (IL-2), IL-4 and C-reactive protein (CRP). (4) Eosinophils including serum eosinophils and sputum eosinophils. (5) Immunoglobulin indices including Immunoglobulin G (IgG), IgA, and IgM. (6) Pulmonary ventilation function indices including forced expiratory volume in one second (FEV1), and FEV1/forced vital capacity (FVC). (7) Incidence rate of adverse reactions.

Statistical analysis

SPSS 26.0 software was utilized for statistical analysis. The numerical data were expressed as n and studied by χ^2 test. The quantitative data were expressed as ($\bar{\chi} \pm s$) and analyzed by *t*-test. P<0.05 suggested that the difference was statistically significant.

RESULTS

Clinical efficacy

The total clinical effective rate was higher in observation group than that in control group (97.14% *vs.* 82.86%, P<0.05) (Table 1).

Table 1. **Clinical efficacy [n (%)]**

Group	n	Cured	Improved	Ineffective	Total effective rate
Control	35	15 (42.86%)	14 (40.00%)	6 (17.14%)	29 (82.86%)
Observation	35	19 (54.29%)	15 (42.86%)	1 (2.86%)	34 (97.14%) *

*P<0.05 *vs.* control group.

Disappearance time of symptoms and signs

The disappearance time of symptoms such as cough and wheezing were shorter in observation group than that in control group (P<0.05), and the disappearance time of pulmonary wheezing sound was shorter in observation group than that in

control group (P<0.05) (Table 2).

Serum inflammatory factors and eosinophils

The levels of IL-2, IL-4 and CRP declined in both groups after treatment in comparison with those before treatment, and they were lower in observation group than those in control group after treatment (P<0.05). The concentrations of eosinophils in sputum and serum declined in both groups after treatment in contrast with those before treatment (P<0.05), and they were lower in observation group than those in control group after treatment (P<0.05) (Table 3).

Table 2. **Disappearance time of symptoms and signs ($\bar{\chi}$ ± s, d)**

Group	Disappearance time of cough	Disappearance time of wheezing	Disappearance time of pulmonary wheezing sound
Control (n=35)	4.73±1.27	3.32±0.83	5.24±1.30
Observation (n=35)	3.60±1.09*	2.41±0.80*	3.92±1.28*

*P<0.05 *vs.* control group.

Table 3. **Serum inflammatory factors and eosinophils ($\bar{\chi}$ ± s)**

Group	Time	IL-2 (pg/mL)	IL-4 (pg/mL)	CRP (mg/L)	Eosinophils in serum (%)	Eosinophils in sputum (%)
Control (n=35)	Before treatment	4.59±0.70	4.08±0.40	9.83±2.35	8.31±1.48	4.25±0.74
	After treatment	3.86±0.61#	3.67±0.35#	7.50±1.87#	6.82±1.20#	3.47±0.62#
Observation (n=35)	Before treatment	4.54±0.72	4.05±0.43	9.71±2.40	8.14±1.53	4.18±0.77
	After treatment	3.25±0.57#*	3.32±0.31#*	5.68±1.49#*	5.63±1.19#*	2.85±0.56#*

#P<0.05 *vs.* before treatment, *P<0.05 *vs.* control group.

Immunoglobulin indices

In comparison with those before treatment, the levels of IgG, IgA and IgM rose in both groups after treatment, and they were higher in observation group than those in control group (P<0.05) (Table 4).

Table 4. **Immunoglobulin indices ($\bar{\chi}$ ± s)**

Group	Time	IgG (g/L)	IgA (g/L)	IgM (g/L)
Control (n=35)	Before treatment	6.10±1.25	1.27±0.23	1.40±0.32
	After treatment	7.89±1.64#	1.51±0.26#	1.78±0.39#
Observation (n=35)	Before treatment	6.15±1.29	1.30±0.21	1.45±0.31
	After treatment	9.73±1.90#*	1.79±0.30#*	2.20±0.43#*

#P<0.05 *vs.* before treatment, *P<0.05 *vs.* control group.

Pulmonary ventilation function indices

Compared with those before treatment, the FEV1 and FEV1/FVC increased in both groups after treatment, and they were higher in observation group than those in control group (P<0.05) (Table 5).

Table 5. **Pulmonary ventilation function indices ($\bar{\chi}$ ± s)**

Group	Time	FEV1 (L)	FEV1/FVC (%)
Control (n=35)	Before treatment	0.85±0.28	32.54±7.34
	After treatment	1.34±0.41#	43.12±9.03#
Observation (n=35)	Before treatment	0.87±0.29	32.69±7.46
	After treatment	1.89±0.53#*	56.94±11.67#*

#P<0.05 *vs.* before treatment, *P<0.05 *vs.* control group.

Incidence of adverse reactions

After treatment, there were 2 cases of headache in observation group and 1 case of nausea in control group. The incidence rate of adverse reactions was 5.71% and 2.86%, respectively, in observation group and control group, without significant difference (P>0.05).

DISCUSSION

Cough variant asthma, also called "cough asthma", is a special type of asthma with chronic cough as the major clinical manifestation. It has a

high morbidity rate and may occur in all age groups. Due to weak autoimmune function, children have a higher risk of cough variant asthma [4,5]. The main symptoms of children with cough variant asthma attack are cough and wheezing. If a child is not treated in time after the attack, the disease will be aggravated, which will easily result in respiratory limitation, severely affecting the health.

The etiology of cough variant asthma is relatively complicated, which is associated with multiple factors. As a special type of asthma, the pathophysiological changes of cough variant asthma are basically the same as that of bronchial asthma, with persistent airway inflammatory response and airway hyperreactivity as the main pathological changes. In clinical practice, patients with cough variant asthma can be treated with reference to the medication for bronchial asthma [6]. Clarityne (loratadine), a kind of antihistamine, has been applied in the treatment of asthma. It can quickly block the binding of histamine to H1 receptor, exerting a good antihistamine effect. Besides, Clarityne can also inhibit platelet activating factor, prostaglandin, mast cells, eosinophils and macrophages, which helps to reduce airway hyperreactivity and control asthma attack. It is often used as an anti-inflammatory drug in the treatment of allergic asthma [7].

Leukotriene receptor, a vital mediator in the pathogenesis of asthma, is involved in the respiratory inflammatory response in patients with asthma [8]. In clinical practice, it is believed that the pathogenesis of cough variant asthma in children is closely associated with leukotriene receptor, and the activation of leukotriene receptor is the major cause of the disease. Hence, leukotriene receptor inhibitors can be used to treat cough variant asthma in children [9]. Singulair (montelukast sodium) is one of the most commonly used leukotriene receptor inhibitors in clinics. It has a strong antagonistic effect against leukotriene receptor and can block the mediation of leukotriene receptor on inflammatory factors, which helps reduce the release of inflammatory factors, alleviating the inflammatory response of respiratory tract. It can also block peptide growth factors from promoting eosinophil maturation and reduce the concentrations of eosinophils in blood and sputum, thereby relieving airway hyperreactivity [10-12]. The results of this study manifested that: (1) The total clinical effective rate was higher in observation group than that in control group (97.14% *vs.* 82.86%, P<0.05). The disappearance time of cough, wheezing and pulmonary wheezing sound was shorter in observation group than that in control group (P<0.05). The levels of IL-2, IL-4 and CRP, and the concentrations of eosinophils in sputum and serum were lower in observation group than those in control group (P<0.05). After treatment, the levels of IgG, IgA and IgM, the FEV1 and FEV1/FVC were higher in observation group than those in control group, indicating that Clarityne combined with Singulair can enhance the anti-inflammatory effect, suppress the airway inflammatory response more effectively, and promote the immune function, thus exhibiting remarkable efficacy. It is mainly because the action mechanisms of the two drugs are different, and the combination of the two drugs can play a good synergistic effect. (2) There was no significant difference in the incidence rate of adverse reactions between observation group and control group (5.71% *vs.* 2.86%, P>0.05), suggesting that Clarityne plus Singulair will not increase the adverse reactions, which has good drug safety.

In summary, Clarityne combined with Singulair has good efficacy in the treatment of cough variant asthma in children. It can effectively relieve the symptoms and signs of children, reduce their inflammatory response, regulate their immune function, and help improve their pulmonary ventilation function. Moreover, the combination of the two drugs leads to few adverse reactions, which is safe and reliable.

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