Effect of Montelukast on Elderly Patients with Bronchial Asthma and Its Effect on Serum Transforming Growth Factor-β1 and Cysteine Leukotriene Levels

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To investigate the effect of montelukast on elderly patients with bronchial asthma and the effects of serum transforming growth factor β1 and cysteinyl leukotriene, 150 patients with bronchial asthma enrolled in the Central Hospital of Shanghai Jingan District between October 2016 to October 2018, and those who met the clinical diagnostic criteria were included. All patients were given antispasmodic and antiinfective treatment after admission. The study group (75 cases) were administered orally montelukast chewable tablets, while the control group (75 cases) was not given montelukast. Comparison of the efficacy of the two groups and lung function indicators before and after treatment, such as 1 second forced expiratory volume, first second forced expiratory volume versus forced vital capacity ratio (1 second forced expiratory volume/versus forced vital capacity), first second forced expiratory volume as predicted percentage and changes in the levels of serum transforming growth factor-β1 and cysteinyl leukotriene. The effective rate of treatment in the study group was higher than that in the control group (93.33 vs. 78.67 %, p<0.05). The first second forced expiratory volume, 1 second forced expiratory volume/versus forced vital capacity and percentage of first second forced expiratory volume/predicted of the study group were significantly increased after treatment (p<0.05), and higher than those of the control group (p<0.05). The levels of transforming growth factor-β1 and cysteinyl leukotriene in the study group were significantly decreased before treatment (p<0.05), and were lower than those in the control group (p<0.05). Montelukast treatment of bronchial asthma in the elderly can significantly improve lung function and improve clinical outcomes. Its mechanism of action may be related to the reduction of transforming growth factor β1 and cysteinyl leukotriene levels.

Key words: Montelukast, old age, bronchial asthma, TGF-β1, Cys-LTs

Bronchial asthma is a chronic allergic disease of the airway. If asthma cannot be effectively relieved for a long time, it can lead to irreversible airway obstruction, poor remodelling, and decreased elasticity of alveoli, emphysema and even heart disease[1]. The elderly patients are often accompanied by osteoporosis, hypertension, diabetes and other basic diseases. The diagnosis and treatment of elderly bronchial asthma has been a big problem in the medical field. Airway inflammation is the main pathogenesis of bronchial asthma. Transforming growth factor-β1 (TGF-β1) and cysteine leukotriene (CysLT) are the main mediators of chronic airway inflammation and airway remodelling. These are also markers of inflammatory reaction and play an important role in the pathogenesis of bronchial asthma[2-3]. Montelukast is a blocker of leukotriene (LT) receptor, which has a significant effect on the treatment of asthma[4].

Inclusion criteria were, all patients in the group met the diagnostic criteria in the guidelines for the prevention and treatment of bronchial asthma[5]. All patients and their families agreed and signed the informed consent. No history of major diseases such as heart disease, liver and kidney dysfunction, tumour, and drug and food allergy. Exclusion criteria were, patients with serious haematological and immunological dysfunction. Patients who have used immunomodulators, glucocorticoids or this study drug in the past 1 mo. Patients with chronic liver and kidney diseases, severe protein energy malnutrition and congenital lung diseases. Those that do not cooperate with the treatment. One hundred and fifty patients were enrolled

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and were divided into the control group and the study group randomly. The baseline data of age, gender and course of disease of the two groups were comparable (p>0.05), as shown in Table 1. This study was approved by the ethics committee of our hospital.

All patients were given symptomatic support treatment after admission, including the treatment of oxygen inhalation, antiinfective therapy, antispasmodic and antiasthmatic drugs. In the study group, oral montelukast was added to the basic treatment, 10 mg once a day for 28 d. Control group received only basic treatment, but not montelukast. Clinical effects were categorised as significant effect if the clinical symptoms such as lung wheeze, wheeze cough and wheeze basically disappeared, first second forced expiratory volume (FEV1) increased by more than 35 % in the first second or FEV1 reached the expected value of 80 %. Effective is when clinical symptoms such as lung wheeze and wheeze cough and wheeze decreased significantly, FEV1 increased by 25-35 % or FEV1 reached the expected value of 60-79 %. Ineffective is when there was no improvement in lung wheeze and wheeze cough or aggravation of clinical symptoms such as cough and wheezing, but no improvement in the decreased FEV1. Clinical effective rate = significant+effective.

According to the American Thoracic Association lung function examination operation specification, the first second forced expiratory volume, the ratio of FEV1 to forced vital capacity (FEV1/FVC), and the percentage of FEV1 to the expected value (PEV1/PRED) were measured. Five millilitres of fasting venous blood was collected in the morning before and after treatment. The supernatant was centrifuged at 3000 rpm in an Eppendorf 5810 centrifuge (Germany) for 10 min and then frozen at -70° in a Sanyo refrigerator (Japan). The levels of TGF-β1 and CysLT were measured using enzyme-linked immunosorbent assay. Adverse reactions of the two groups were monitored during the treatment. SPSS25.0 is used for data analysis. The measurement data with homogeneity and normality of variance tested by K-S method are represented by t test. Rate (%) indicates that the counting data is tested by 2, and the grade data is tested by Kruskal Wallis H. p<0.05: the difference was statistically significant.

The effective rate of treatment in the study group was higher than that in the control group (p<0.05), as shown in Table 2. There was no difference in FEV1, FEV1/FVC and PEV1/PRED between the two groups before treatment (p>0.05). After treatment, FEV1, FEV1/FVC and PEV1/PRED increased (p<0.05). After treatment, FEV1, FEV1/FVC and PEV1/PRED in the study group were higher than those in the control group (p<0.05), as shown in Table 3. There was no difference in serum TGF-β1 and Cys lts levels between the two groups before treatment (p>0.05). After treatment, the serum TGF-β1 and CysLT levels decreased (p<0.05). After treatment, the serum TGF-β1 and CysLT levels in the study group were lower than those in the control group (p<0.05), as shown in Table 4. There was no obvious damage of liver and kidney function and no drug-related adverse reactions.

TABLE 1: PATIENT GENERAL INFORMATION

Project	Research Group (75)	Control group (75)	t/χ^2	P
Gender (%)				
Male	41 (54.67)	45 (60.00)	0.436	0.509
Female	34 (45.33)	30 (40.00)		
Age (y)	66.82±5.61	65.02±6.93	1.748	0.082
Course of disease (y)	3.15±1.09	3.27±1.28	0.618	0.537
Asthma grading				
Light	43 (57.33)	44 (58.67)	0.027	0.869
Moderate	32 (42.67)	31 (41.33)		

TABLE 2: PERCENT CLINICAL EFFECTS

Group	Case	Markedly effective	Effective	Ineffective	Total effective
Study Group	75	45 (60.00)	25 (33.33)	5 (6.67)	70 (93.33)
Control group	75	29 (38.67)	30 (40.00)	16 (21.33)	59 (78.67)
χ^2					6.700
P					0.010

TABLE 3: THE DIFFERENCE OF FEV1, FEV1/FVC AND PEV1/PRED BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT

	Research group (75 cases)				Control group (75 cases)				P1	P2
	Before treatment	After treatment	t	P	Before treatment	After treatment	t	P		
FEV1 (L)	1.53±0.69	1.95±0.53	4.181	0.000	1.55±0.71	1.80±0.21	2.924	0.004	0.861	0.024
FEV1/FVC (%)	56.92±13.67	72.52±15.82	6.462	0.000	59.05±13.06	66.13±14.34	3.161	0.002	0.331	0.011
PEV1/PRED (%)	49.53±10.25	65.26±17.67	6.669	0.000	50.06±11.64	58.26±15.43	3.674	0.000	0.768	0.011

Note: P1 is the statistical value of the two groups before treatment; P2 is the statistical value of the two groups after treatment

TABLE 4: THE DIFFERENCE OF SERUM TGF-β1 AND CysLT BETWEEN THE TWO GROUPS BEFORE AND AFTER TREATMENT

Target	Research group (75 cases)				Control group (75 cases)				P1	P2
	Before treatment	After treatment	t	P	Before treatment	After treatment	t	P		
TGF-β1 (pg/ml)	146.25±43.98	70.25±29.34	12.449	0.000	147.13±45.25	95.36±32.64	8.036	0.000	0.904	0.000
Cys-LT (pg/ml)	185.25±35.61	102.35±16.54	18.285	0.000	186.29±35.69	126.35±29.67	11.184	0.000	0.858	0.000

Note: P1 is the statistical value of the two groups before treatment; P2 is the statistical value of the two groups after treatment

Bronchial asthma is characterized by airway hyper responsiveness, which is involved by many kinds of cells and cell components. The patients often show a wide range of reversible symptoms such as airflow restriction, wheezing, shortness of breath, chest tightness and/or cough[6]. Bronchial asthma is a common chronic respiratory disease in the world. With the aggravation of environmental pollution, the incidence of bronchial asthma is increasing, which has become a global public health problem[7]. Asthma is a widespread and reversible airway stenosis disease caused by allergens or other factors. It can attack within minutes and last for hours to days. Bronchodilators are effective or can relieve themselves. The pathogenesis of bronchial asthma is still unclear. The existing research considers that asthma is a disease with family aggregation tendency and polygenic heritage background[8]. The disorder of airway autonomic nerve function is the pathophysiological basis leading to airway hyper responsiveness[9]. Inflammatory mediators, EOS, mast cells, living platelets, all participate in the formation of airway inflammation.

TGF-β1 is a multifunctional cell regulatory factor. In the pathological process of asthma, TGF-β1 can be used as an inflammatory factor to start the chronic inflammatory response of the airway, promote the mitosis and proliferation of airway fibrocytes, cause airway fibrosis and remodelling, and aggravate asthma[10]. LT is an important inflammatory factor, which can promote the synthesis and release of inflammatory cytokines. It tends to infiltrate and activate inflammatory cells in the airway, forming chronic airway inflammation, causing the contraction of bronchial smooth muscle and promoting the inflammatory response. Previous studies have shown that CysLT participates in the airway inflammation of asthma[11]. The levels of TGF-β1 and LTE4 are closely related to the severity of asthma in children with acute attack. They are important observation indexes for clinical monitoring of asthma, evaluation of curative effect and judgment of prognosis[12].

Montelukast is a highly effective and selective LT receptor antagonist. By combining with LT receptor in airway smooth muscle cells, montelukast can block the production of LT polypeptide, improve airway permeability, increase mucus secretion, inhibit eosinophil and basophil infiltration, reduce airway inflammation, high reactivity and remodelling, improve lung function and alleviate asthma symptoms[13]. Existing research shows that montelukast can effectively reduce the level of LT's in children with asthma, control the acute attack of asthma, and reduce the recurrence[14,15]. This study shows that montelukast has a reliable clinical effect in the treatment of elderly bronchial asthma, which is superior to the basic treatment, and can significantly improve the lung function of patients. During the treatment, there is no serious drug-related adverse reaction, and the safety is high. In this study, we observed the effect of montelukast on the levels of TGF-β1 and CysLT, and found that montelukast has a good inhibitory effect on the levels of TGF-β1 and CysLT, suggesting that montelukast may play a role in the treatment of asthma by inhibiting the levels of TGF-β1 and CysLT. However, the specific mechanism still needs further clinical research.

In summary, montelukast treatment of elderly patients with asthma can significantly improve lung function and improve clinical efficacy. The mechanism may be related to the decrease of TGF-β1 and CysLT. Since no further mechanism study has been carried out in this study, the mechanism of montelukast in the treatment of bronchial asthma remains to be confirmed by more clinical studies.

Conflict of interest:

There was no conflict of interest.

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