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Research on Role of Regulatory Polypeptide Ac-Sdkp in Restraining Silicosis Fibrosis

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Abstract: Objective: To explore the specific role of regulatory polypeptide Ac-SDKP in restraining silicosis fibrosis. Methods: The study starts from February 2020 to February 2021. 20 Wistar rats are selected as subjects of the study, and they are randomly divided into treatment group and model group. The treatment group is treated with anti-fibrosis of regulatory polypeptide Ac-SDKP, while the model group is not treated. And the expressions of p-CREB, PKA, and cAMP in the two groups of rats are observed. Results: The expressions of p-CREB, PKA and cAMP in the treatment group are higher than those in the model group ($P < 0.05$). Conclusion: Silicosis fibrosis can be inhibited by the regulatory polypeptide Ac-SDKP.

1. Introduction

Silicosis is an occupational lung disease. The main cause of its occurrence is that patients inhale silicon dioxide during long-term production activities. Pulmonary fibrosis and silicosis are the main pathological changes of silicosis. Myofibroblasts and extracellular matrix are formed in the process of pulmonary fibrosis. Therefore, the treatment of silicosis fibrosis needs to focus on how to control the transformation of myofibroblasts [1]. In this study, rats are selected to analyze the effects of treatment with regulatory polypeptide Ac-SDKP. The specific content is described as follows.

2. Information and Methods

2.1 General Information

The study starts from February 2020 to February 2021. 20 Wistar rats are selected as subjects of the study, and they are randomly divided into treatment group and model group. Both of the two groups contain 10 rats, each of which is 3 weeks old and weighs in the range of (50±10) g.

Inclusion criteria: (1) All rats are from Beijing Weitong Lihua Company. (2) All rats are male.

Exclusion criteria: (1) the rat has a disease. (2) The source information of the rat is imperfect.

2.2 Methods

The Ac-SDKP used in this study is from Bachem AG in Switzerland, and the drug micro-release pump is purchased from DURECT in the United States, p-CREB primary antibody from Abcam in the United States, and cAMP primary antibody from Eterlife in the United Kingdom, and PKA from

Bailey Biotechnology Company in Shanghai of China.

The rats in the model group are exposed to dust for 3 hours a day with the help of the HOPE-MED8050 exposure cabinet for up to 16 weeks. After the rats in the treatment group are exposed to dust for 4 weeks, the relevant personnel bury a micro-scale sustained-release pump containing Ac-SDKP [800μg/(kg·d)] into the abdominal cavity of the rats, and the rats continue to be exposed to dust up to 16 weeks.

After 16 weeks, the lung tissues of the two groups of rats are observed and Western Blot is performed. The specific steps for observing the morphology of lung tissue are to take the right lower lung of the rat and fix it under 4% paraformaldehyde, and embed it in paraffin. After VG staining, the lung fibrosis and collagen fiber deposition of the rats can be effectively observed. The specific method of Western Blot detection is to extract the protein from the lung tissue of rats, take the protein for loading, electrophoresis, and electroporation, add p-CREB, PKA, and cAMP respectively to incubate overnight at 4°C, and add the corresponding two anti-antibody to incubate at 37°C for 30 minutes, perform ECL development, and perform image scanning in a gel imaging system.

2.3 Observation Indexes

The expressions of p-CREB, PKA and cAMP in the treatment group and model group are observed.

2.4 Statistical Methods

SPSS 24.0 is used as a data analysis tool in this study, and mean ± standard deviation are used to reflect the measurement data, t value are referred as the test value. When $P < 0.05$, it shows that the research data has statistical significance.

3. Results

The value of p-CREB, PKA and cAMP in the treatment group are higher than those in the model group ($P < 0.05$). The detailed data are shown in Table 1.

Table 1 Comparison of Value of P-Creb, Pka, Camp (X ± s,Wb)

Group	Case	p-CREB	PKA	cAMP
The treatment group	10	1.33±0.26	0.62±0.10	0.46±0.06
The model group	10	0.28±0.10	0.12±0.06	0.21±0.05
t	--	8.362	7.329	8.136
p	--	0.001	0.001	0.001

4. Discussion

Silicosis is a diffuse fibrosis of the lungs caused by long-term inhalation of quartz dust. Symptoms of silicosis mainly include cough, chest tightness and dyspnea. But it sometimes has no significant symptoms. The main characteristics of silicosis are lung inflammation and progressive pulmonary fibrosis. With the further development of pulmonary fibrosis, lung function is impaired and the gas exchange area is reduced, which directly causes respiratory failure, and even lung cancer in severe cases. Silicosis fibrosis has a high mortality rate in clinical practice, so patients should be treated as soon as possible to alleviate the condition.

At present, the main treatment measures for silicosis are lung lavage, anti-pulmonary fibrosis,

and improving the body's resistance. Although various drugs and non-drug interventions have been used, the existing treatment methods still cannot effectively alleviate the development of the disease and reverse pulmonary fibrosis. Effective clinical measures should be taken to restrain silicosis fibrosis [2-3].

In silicosis fibrosis, the proliferation, differentiation and metastasis of fibroblasts are related to many different cell signal pathways and transduction pathways, among which the more common signal transduction pathways are PDGF/ROCK and P38. Ac-SDKP can significantly reduce the expression of type I and type III collagen in silicosis rats, resulting in an effective reduction in the expression of TGF-β1 in the lungs of rats. Ac-SDKP can significantly inhibit pulmonary fibrosis. In the early stage of AS, patients with hypercholesterolemia will have hypercholesterolemia. Monocytes will adhere to fibrocytes more obviously, and monocytes will also migrate between endothelial cells with the help of chemotaxis. P38 will be stimulated by oxidized low-density lipoprotein to secrete MMPS, so that P38 will degrade the extracellular matrix components of fibroblast blocks as soon as possible, further enhancing the vulnerability of plaques, and its specific level determines the severity of ACS to a certain extent. . In addition, related clinical studies have shown that the parts with a larger area of fibroblast clumps have higher P38 content, which can indicate that P38 infiltration participates in the formation of fibroblast clumps. Matrix metalloproteinases have a significant regulatory role in the occurrence of silicosis. The composition of matrix metalloproteinases is a specific protein. The concentration of MMP-9 in the peripheral blood of ACS patients will increase, which is related to the stability of plaques. , Clinically, the level of MMP-9 can be used to predict the vulnerability of plaque. Ac-SDKP can reduce the expression level of angiotensin receptor, TGF-β1 and its receptor, reduce the further deposition of collagen, and effectively reduce the differentiation of lung fibroblasts, thereby reducing the content of lung fibroblasts and avoiding Silicosis appeared.

The regulatory polypeptide Ac-SDKP is composed of four amino acids, namely N-acetyl-seryl-aspartyl-lysyl-proline. There are clinical related studies showing that Ac-SDKP can play its role in TGF - β 1- β/ Smad pathway and significantly slow down the progression of diabetic myocardial fibrosis in rats and protect renal interstitial fibrosis to a certain extent. Ac-SDKP can reduce the phosphorylation of Smad2 in embryonic myocardial fibroblasts, restrain the proliferation of fibroblasts and myofibroblast transformation. cAMP can speed up the activation of PKA, can promote the phosphorylation of CREB at serine 133, can speed up the translocation of p-CREB into the nucleus, and play a good regulatory role in the expression of related proteins [4-5]. At the same time, there are related clinical studies showing that CREB, PKA, and cAMP signal pathways have the effects of anti-liver fibrosis. The results of this study show that the p-CREB, PKA, and cAMP of the rats in the treatment group are higher than those in the model group, which indicates that Ac-SDKP can effectively activate p-CREB, PKA, and cAMP signals. The activation of p-CREB, PKA and cAMP can effectively resist myofibroblast transformation in the process of silicosis fibrosis in rats.

By summarizing the above contents, we can know that in the clinical treatment of silicosis, the regulatory polypeptide Ac-SDKP can be used to effectively regulate silicosis fibrosis, so that myofibroblast transformation can be significantly inhibited, and the patient's condition can be well controlled.

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