THE EXPRESSION OF IFN - Γ, IL-10, IL-12 AND CCL1 IN PATIENTS WITH PULMONARY TUBERCULOSIS

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ABSTRACT

Objective*: This study explored the expression of IFN-γ, IL-10, IL-12 and CCL1 in patients with pulmonary tuberculosis and their significance.*

Methods: *From November 2016 to February 2018, 31 patients with pulmonary tuberculosis in our hospital were collected as the experimental group, and 31 healthy volunteers who were examined in our hospital in the same period, were collected as the control group. The levels of IL-6, IL-10, IL-12, IFN-γ, MCP-1 and CCL1 were analysed. The changes of IL-10, IL-12, IFN-γ and CCL1 were analysed after the treatment.*

Results: *Compared with the control group, the levels of IL-10, IL-12, IFN-γ and CCL1 in the experimental group were significantly higher (p<.05). After treatment, the levels of IL-10, IL-12, IFN-γ and CCL1 in the experimental group were significantly reduced (p<.05). Compared with the control group, the levels of IL-6 and MCP-1 in the experimental group were significantly higher (p<.05). A correlation analysis showed that IL-10 was positively correlated with IL-12, IFN-γ, CCL1, IL-10 and MCP-1.*

Conclusion: *The levels of IFN-γ, IL-10, IL-12 and CCL1 in the serum of patients with pulmonary tuberculosis are significantly increased, and there is immune impairment. This has important implications for the prevention and treatment of tuberculosis, and it is expected to become the reference for clinical diagnosis and prognosis evaluation of tuberculosis.*

Keywords: *Tuberculosis, IFN-γ, IL-10, IL-12, CCL1.*

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Introduction

Tuberculosis is a respiratory infectious disease caused by the pathogen Mycobacterium tuberculosis that can lead to death. Most infected people are in the incubation period and do not show obvious symptoms. About 10% of infected people become symptomatic patients with tuberculosis[1]. Mycobacterium tuberculosis can invade many organs in the body, especially the lungs, and it seriously threatens patients' health and social interactions[2]. At present, tuberculosis cases in China account for 14% of cases worldwide, and the incidence is second to India. In addition, factors such as inadequate management of the disease in many countries have led to increased drug resistance in tuberculosis patients, so the number of patients has increased[3]. In recent years, a great deal of reporting and surveillance of infectious diseases has revealed that the incidence of tuberculosis is still high. It has the characteristics of large infection base, a large number of infected people, enhanced drug resistance and low coverage of directly observed treatment short course (DTOS).

This has created serious problems for the prevention and treatment of tuberculosis[4]. The inflammatory and allergic reactions in patients with pulmonary tuberculosis act on the body at the same time, resulting in the decline of immune function and tis-

sue destruction[5]. In recent years, studies have confirmed that cytokines play a significant role in the pathogenesis of tuberculosis, and their expression is of great significance to the onset, progress and evolution of tuberculosis. Interferon gamma (IFN-γ) can participate in immune regulation and enhance the response of the body, but it does not kill or inhibit the virus directly[6]. Clinical studies have shown that the pro-inflammatory factor Interleukin-12 (IL-12) and the anti-inflammatory factor Interleukin-10 (IL-10) play important roles in tuberculosis[7].

Chemokine cytokine ligand 1 (CCL1), as an inflammatory mediator, can play a role in binding to CCR receptors in tuberculosis[8]. Therefore, this study investigates the significance of these factors on tuberculosis by detecting the expression of IFN-γ, IL-10, IL-12, and CCL1 in the serum of patients with tuberculosis.

Data and methods

General information

From November 2016 to February 2018, 31 patients with tuberculosis in our hospital were selected as the experimental group. There were 14 males and 17 females with an average age of (35.61±15.41) years.

Admission criteria were:

• All the participants met the diagnosis criteria of tuberculosis in the guidelines for diagnosis and treatment of tuberculosis and confirmed by professional doctors;

• Their diagnosis was confirmed by chest X-ray and sputum concentration pictures;

• They had complete pathological data;

• They knew the content of the experiment and signed an informed consent form.

• They applied to the hospital ethics committee and got approval.

Exclusion criteria were:

• Recent use of glucocorticoids or immunosuppressants;

• Except tuberculosis, all lung diseases that can cause the increase or decrease of IFN-γ, IL-10, IL-12 and CCL1 in serum;

• Malnutrition, mental disorder or poor compliance.

The control group comprised 31 healthy volunteers. There were 16 males and 15 females with an average age of (34.93±16.12) years. There was no significant difference in general data between the two groups (p>.05).

Method

• In the experimental group, 5 ml of fasting venous blood was extracted in the early morning after admission and centrifuged at 1500 R·min-1 for 20 minutes. The supernatant was stored in an ultra-low temperature refrigerator;

• In the control group, 5 ml of fasting venous blood was drawn on the day of physical examination. The other steps were the same as those in the experimental group;

• The patients in the experimental group received routine chemotherapy for tuberculosis. After the treatment, the venous blood of the patients was drawn again in the early morning for detection.

Observation indicators

The levels of IFN-γ, IL-6, IL-10, IL-12, CCL1 and monocyte chemoattractant protein 1 (MCP-1) were detected by enzyme-linked immunosorbent kit (produced by Shanghai Yiyan Biotechnology Co., Ltd.), and the correlation among the cytokines was analysed.

Statistical methods

The serum levels of cytokines IFN-γ, IL-10, IL-12 and CCL1 in each group were expressed by $\bar{x}\pm s$. The differences between groups were analysed by one-way ANOVA. And t-test was used for comparison between the two groups. The correlation between the cytokines in patients with pulmonary tuberculosis was analysed by Pearson. SPSS 23.0 was used to analyse the data of each group. A p<.05 means that the difference was significant.

Results

Comparison of IL-10, IL-12, IFN-γ and CCL1 levels in each group

Compared with the control group, the levels of IL-10, IL-12, IFN-γ and CCL1 in the experimental group were significantly higher (p<.05), as seen in Table 1.

Group	n	IL-10 (pg/mL)	IL-12 (pg/mL)	IFN-γ (pg/mL)	CCL1 (μg/L)
Control group	31	82.58±31.40	9.54±0.33	90.91±2.16	159.14±29.32
Experience group	31	172.24±77.54	15.07±0.69	116.26±5.07	382.71±30.10
t		5.967	40.256	25.611	29.624
p		< .001	< .001	< .001	< .001

Table 1: Comparison of IL-10, IL-12, IFN-γ and CCL1 Levels in Each Group ($\bar{x}\pm s$).

Changes of IL-10, IL-12, IFN-γ and CCL1 levels in patients with pulmonary tuberculosis after treatment

After treatment, the levels of IL-10, IL-12, IFN-γ and CCL1 in the experimental group were significantly reduced (p<.05), as seen in Table 2.

Group	Time	IL-10 (pg/mL)	IL-12 (pg/mL)	IFN-γ (pg/mL)	CCL1 (μg/L)
Experimental group	Before treatment	172.24±77.54	15.07±0.69	116.26±5.07	382.71±30.10
	After treatment	93.68±35.12	12.01±0.36	98.56±4.56	246.13±33.15
t		5.136	21.891	14.452	16.983
p		< .001	< .001	< .001	< .001

Table 2: Changes of IL-10, IL-12, IFN-γ and CCL1 levels in patients with pulmonary tuberculosis after treatment ($\bar{x}\pm s$).

Comparison of IL-6 and MCP-1 levels in each group

Compared with the control group, the levels of IL-6 and MCP-1 in the experimental group were significantly higher (p<.05), as seen in Table 3.

Group	n	IL-6 (pg/mL)	MCP-1 (ng/mL)
Control group	31	0.54±0.04	198.52±20.43
Experimental group	31	0.97±0.05	252.12±64.81
t		37.390	4.392
p		< .001	< .001

Table 3: Comparison of IL-6 and MCP-1 levels in each group ($\bar{x}\pm s$).

Correlation analysis of cytokines in patients with pulmonary tuberculosis

The correlation analysis showed that IL-10 was positively correlated with IL-12, IFN-γ, CCL1, IL-6 and MCP-1, as seen in Table 4.

Cell factor	IL-10	IL-12	IFN-γ	CCL1	IL-6	MCP-1
IL-10	-	0.548	0.824	0.634	0.741	0.659
IL-12	0.545	-	0.654	0.543	0.562	0.666
IFN-γ	0.562	0.525	-	0.777	0.888	0.526
CCL1	0.656	0.653	0.635	-	0.567	0.894
IL-6	0.712	0.895	0.852	0.589	-	0.873
MCP-1	0.856	0.589	0.654	0.863	0.698	-

Table 4: Correlation analysis of cytokines in patients with pulmonary yuberculosis. ($\bar{x}\pm s$).

Discussion

Pulmonary tuberculosis is often combined with symptoms of poisoning, especially fever. In addition, symptoms such as cough, sputum, and tuberculosis allergy are strong indicators of the possibility of tuberculosis. At the initial stage of tuberculosis, pulmonary signs are not significant and not specific, but as the disease progresses, corresponding signs appear. The form of tuberculosis control in China is extremely severe, and its occurrence is related to the size of pathogenic bacteria to a certain extent. The level of the body's autoimmune ability and the relative stability of immune cytokines can regulate the anti-tuberculosis immune response and immune regulation. It has been reported that macrophages can clear pathogenic bacteria through the body's network system, and they can be used as a resistance barrier[9]. In this experiment, macrophage-related factors IFN-γ, IL-10, IL-12, and CCL1 were selected for detection, and the clinical significance of these factors in the immune response to tuberculosis was further analysed.

IL-10 is the anti-inflammatory factor with the function of mediating immunosuppression. As the body is infected with Mycobacterium tuberculosis, it can inhibit the uptake of dendritic cells and inhibit the type 1 polarization of helper T cell subsets caused by IFN-γ[10]. When IL-10 and other anti-inflammatory factors are released in excess, immunosuppression may result. This reduces the body's ability to eliminate Mycobacterium tuberculosis, leading to further deterioration of the disease. IL-12 is the important pro-inflammatory factor to maintain the immune memory and immune balance of the body. After the body is infected with Mycobacterium tuberculosis, IL-12 can enhance the immune response mediated by the helper T cell subpopulation type 1 cells, closely linking the natural immune closely linked with the specific immune, and providing its anti-Mycobacterium tuberculosis function[11]. IFN-γ is the protective cytokine with strong regulatory function. It has been reported that increasing the level of IFN-γ in the body after infection with Mycobacterium tuberculosis suggests that the patient's condition is more serious and with the increase of protective immunity[12].

Other studies have shown that the patient's condition will be alleviated with a decrease in the lever of random IFN-γ with the timely and effective treatment of tuberculosis patients[13]. In addition, studies have shown that the level of IFN-γ in Tibetan tuberculosis patients was significantly higher than the control group and that IFN-γ participates in the immune response when the body is infected with Mycobacterium tuberculosis[14]. An interferon gamma release test in vitro has been used in clinical practice, and it

has become an important means for clinical workers to assist in the diagnosis of tuberculosis[15]. The role of IL-6 in pulmonary tuberculosis is similar to that of IL-12 in that both of them are pro-inflammatory factors[16-17]. IL-6 can promote the differentiation of B cells and form antibodies, further activate T cells and promote their proliferation, and play an inflammatory role in the immune response of the body[18-19]. MCP-1 has strong chemotaxis on monocytes. In the early stage of infection with Mycobacterium tuberculosis, MCP-1 can form and release rapidly. At the same time, the monocyte macrophages can gather in the inflammatory site and play an anti-tuberculosis role via an immune response. Tuberculosis-related research shows that overexpression of MCP-1 can increase the susceptibility of tuberculosis patients and hinder the release of IL-12[20].

In this experiment, macrophage-related factors were measured by enzyme-linked immunosorbent assay, to explore the changes in the levels of cytokines leading the occurrence of tuberculosis, and to provide a reference for determining the severity of tuberculosis and immunosuppressive therapy. Compared with the control group, the levels of IL-10, IL-12, IFN-γ and CCL1 in the experimental group were significantly higher ($p<.05$). After treatment, the levels of IL-10, IL-12, IFN-γ and CCL1 in the experimental group were significantly reduced ($p<.05$). Compared with the control group, the levels of IL-6 and MCP-1 in the experimental group were significantly higher ($p<.05$). The analysis showed that IL-10 was positively correlated with IL-12, IFN-γ, CCL1, IL-6 and MCP-1. These results suggest that the inflammatory response is further aggravated by the progress of tuberculosis. These factors play an important role in the immunopathology of local tissues infected with tuberculosis. The change of IFN-γ level can directly regulate the level of immunity. The change of MCP-1 level is closely related to the course of tuberculosis.

Thus, the levels of IFN-γ, IL-10, IL-12 and CCL1 in the serum of patients with pulmonary tuberculosis are significantly increased, and this is accompanied by the phenomenon of immune impairment. This is of great significance for the prevention and treatment of pulmonary tuberculosis, and it is expected to be the reference for clinical diagnosis and prognosis of pulmonary tuberculosis.

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