ANALYSIS ON DIFFERENCES OF IL-1P, TNF-A, IP-10, MCP-1 AND MIP-1P EXPRESSIONS IN PLASMAS OF BRONCHIAL AND PULMONARY TUBERCULOSIS PATIENTS AND HEALTHY PEOPLE

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ABSTRACT

Objective: *To investigate the expression differences of IL-1p, TNF-α, IP-10, MCP-1, MIP-1pin plasma among bronchial tuberculosis patients, pulmonary tuberculosis patients and healthy people.*

Methods: *From April 2013 to April 2017, 63 cases of bronchial tuberculosis, 67 cases of pulmonary tuberculosis, 65 healthy check-up in our hospital were the research object. Corresponding elisa kits were used to detect the concentration of the IL-1p, TNF-α, IP-10, MCP-1, MIP-1pin plasma of the bronchial tuberculosis, pulmonary tuberculosis, healthy check-up crowd, the detection indexes were analysed by T test and Person correlation analysis about difference and correlation analysis.*

Results: *The content of IL-1p, TNF-α, IP-10, MCP-1, MIP-1pin plasma among bronchial tuberculosis patients were higher than healthy check-up crowd, and the various testing indexes had significant difference between two groups (P<0.05). The content of IL-1p, TNF-α, IP-10, MCP-1, MIP-1pin plasma among pulmonary tuberculosis patients were higher than healthy check-up crowd, and the various testing indexes had significant difference between two groups (P<0.05). The content of IL-1p, TNF-α, IP-10, MCP-1, MIP-1pin plasma of bronchial tuberculosis patients were almost as same as pulmonary tuberculosis patients, and the various testing indexes had no significant difference between two groups (P>0.05). The content of IL-1p was positively related with TNF-α in bronchial tuberculosis patients (r=0.903, P=0.018), and The content of IL-1p was positively related with IP-10, MCP-1, MIP-1p (r=0.917, P=0.017; r=0.889, P=0.021; r=0.856, P=0.019). Also, The content of IL-1p was positively related with TNF-α in pulmonary tuberculosis patients (r=0.921, P=0.013), and The content of IL-1p was positively related with IP-10, MCP-1, MIP-1p (r=0.894, P=0.012; r=0.901, P=0.015; r=0.878, P=0.023).*

Conclusion: *The contents of IL-1p, TNF-α, IP-10, MCP-1, MIP-1pin plasma of Patients with bronchial tuberculosis and pulmonary tuberculosis all had significant differences with the healthy people. So we could use those indexes as auxiliary indexes when we diagnosed bronchial tuberculosis and tuberculosis to achieve the best treatment period for patients.*

Keywords: *bronchial tuberculosis, pulmonary tuberculosis, IL-1p, TNF-α, IP-10, MCP-1, MIP-1p.*

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Introduction

All over the world, tuberculosis caused by tuberculosis mycobacteria is one of the diseases with the highest death and infection rates[ß]. China is one of the countries with the highest occurrence rate of tuberculosis in the world and the tuberculosis has seriously affected the health of Chinese people and become one of critical diseases highly concerned in China[(2)]. Bronchial tuberculosis and pulmonary tuberculosis care caused by tuberculosis mycobacteria, the bronchial tuberculosis occurs quickly and the pulmonary tuberculosis is long-lasting and is easy to be infected repeatedly and have drug-resistance. So far, there is no gold standard for diagnosis of bronchial tuberculosis and pulmonary tuberculosis, which is mainly diagnosed by observing whether lesion is discovered in tissues or the tuberculosis mycobacteria are found out in sputum or case samples. So, the diagnosis is fuzzy and may be wrong easily, finally losing the best treatment time. Therefore, early and accurate diagnosis of bronchial tuberculosis and pulmonary tuberculosis is quite important for early treatment. In the immune system, the body gives play to the immunoregulation via inflammatory factors - interleukins IL-1p and

TNF-α[3], and the chemotactic factors IP-10, MCP-1 and MIP-1p are possibly related to the pathologic tissues. This article discusses the expression differences of inflammatory factors IL-1p and TNF-α and chemotactic factors IP-10, MCP-1 and MIP-1p in blood plasma of the healthy people and the bronchial and pulmonary tuberculosis patients, so as to find a simple, rapid and accurate inspection means for bronchial and pulmonary tuberculosis.

Materials and methods

Subjects Investigated

The subjects included: 63 bronchial tuberculosis patients (male: 35; female: 28) with the age of 23-57 and mean age of 37.5±4.3; 67 pulmonary tuberculosis patients (male: 31; female: 36) with the age of 26-55 and mean age of 35.6±5.1; 65 healthy people (male: 34; female: 31) with the age of 25-56 and mean age of 37.1±4.7, who were confirmed in our hospital from April 2013 to April 2017. Blood sampling was done for all subjects before treatment.

Inclusion standards: bronchial and pulmonary tuberculosis patients: sputum bacterioscopy indicated that tuberculosis mycobacteria were positive and pathologic tissue testing showed symptoms of tuberculosis infection; healthy people: sputum bacterioscopy indicated negative tuberculosis mycobacteria and there was no tuberculosis-infected tissue. All subjects concluded relevant contracts.

Exclusion standards: HIV, HCV, TP, HBV and other communicable disease patients, malignant tumor patients, pregnant and breast-feeding women, as well as the patients with relevant immune diseases or taking relevant immune drugs.

Research Method

Blood Sampling: For all subjects, 10ml venous blood was taken with EDTA anticoagulation blood sampling tubes before the treatment and centrifuged at 3000r/min for 10min, and then supernatant was taken and saved under -20 oC.

T*esting Indicators and Methods:* Testing indicators included the concentrations of inflammatory factors IL-1p and TNF-α and chemotactic factors IP-10, MCP-1 and MIP-1p in blood plasma of bronchial and pulmonary tuberculosis patients and healthy people.

All testing indicators were tested with relevant ELISA kits strictly according to the operating requirements specified on the specifications. IL-1p assay kit was bought from American Cloud Clone Company, TNF-α assay kit from American R&D Company and IP-10, MCP-1 and MIP-1p assay kits from American eBioscience Company.

Statistical Analysis

The investigational data were analyzed with SPSS18.0 and indicated in mean value ± standard deviation ($\bar{x}$±s), inter-group data were analyzed by T-test, and relevancy was analyzed by Pearson, of which P<0.05 was considered as the data were significantly different.

Results

Analysis of Testing Indicators of Bronchial Tuberculosis Patient and Healthy People

It could be seen from Table 1 that IL-1p, TNF-α, IP-10, MCP-1 and MIP-1p contents in blood plasma of bronchial tuberculosis patients were higher than those of the healthy people. In addition, the differences of all testing indicators were significant between two groups (P<0.05).

Group	Bronchial tuberculosis patient	Healthy people
IL-1p (pg/ml)	1.52±0.89*	0.77±0.23
TNF-α (ng/L)	91.47±7.02*	31.88±2.78
IP-10 (ng/L)	243.48±31.26*	43.69±10.28
MCP-1 (pg/ml)	653.21±103.34*	104.35±34.27
MIP-1p (pg/ml)	478.37±57.89*	132.13±37.21

Table 1: Comparison of IL-1p/TNF-α/IP-10/MCP-1/MIP-1p between Patients with bronchial tuberculosis and healthy people.
*Compared between two group, *P<0.05.*

Analysis of Testing Indicators of Pulmonary Tuberculosis Patient and Healthy People

It could be seen from Table 2 that IL-1p, TNF-α, IP-10, MCP-1 and MIP-1p contents in blood plasma of pulmonary tuberculosis patients were higher than those of the healthy people. In addition, the differences of all testing indicators were significant between two groups (P<0.05).

Group	Bronchial tuberculosis patient	Healthy people
IL-1p (pg/ml)	1.47±0.66*	0.77±0.23
TNF-α (ng/L)	93.31±6.92*	31.88±2.78
IP-10 (ng/L)	256.37±34.01*	43.69±10.28
MCP-1 (pg/ml)	643.55±99.97*	104.35±34.27
MIP-1p (pg/ml)	481.37±53.74*	132.13±37.21

Table 2: Comparison of IL-1p/TNF-α/IP-10/MCP-1/MIP-1p between Patients with pulmonary tuberculosis and healthy people.
*Compared between two group, *P<0.05.*

Analysis of Testing Indicators of Bronchial and Pulmonary Tuberculosis Patients

It could be seen from Table 3 that IL-1p, TNF-α, IP-10, MCP-1 and MIP-1p contents in blood plasma of bronchial and pulmonary tuberculosis patients were almost similar. In addition, the differences of all testing indicators were not significant between two groups (P>0.05).

Group	Bronchial tuberculosis patient	Healthy people
IL-1p (pg/ml)	1.52±0.89	1.47±0.66
TNF-α (ng/L)	91.47±7.02	93.31±6.92
IP-10 (ng/L)	243.48±31.26	256.37±34.01
MCP-1 (pg/ml)	653.21±103.34	643.55±99.97
MIP-1p (pg/ml)	478.37±57.89	481.37±53.74

Table 3: Comparison of IL-1p/TNF-α/IP-10/MCP-1/MIP-1p between Patients with bronchial tuberculosis and pulmonary tuberculosis .
*Compared between two group, *P<0.05.*

Relevancy Analysis

From Person relevancy analysis, it could be seen that IL-1p and TNF-α in blood plasma of bronchial tuberculosis patients were in positive correlation (r=0.903, P=0.018) and they were also in positive correlation with IP-10, MCP-1 and MIP-1p (r=0.917, P=0.017; r=0.889, P=0.021; r=0.856, P=0.019).

In a similar way, Person relevancy analysis was done for all indicators in blood plasma of pulmonary tuberculosis patients and the results showed that IL-1p and TNF-α were in positive correlation (r=0.921, P=0.013) and they were also in positive correlation with IP-10, MCP-1 and MIP-1p (r=0.894, P=0.012; r=0.901, P=0.015; r=0.878, P=0.023)

Discussion

At present, tuberculosis is one of the diseases with higher infection rate, incidence rate and death rate in China. The people infected with tuberculosis mycobacteria is increasing gradually every year and the bronchial and pulmonary tuberculosis patients increased year by year as well, and they have seriously affected living health of the human being. The infectious positions of bronchial tuberculosis are bronchial or tracheal mucous membrane, submucosa, muscular layer, cartilage and other histological structures[4]. The infected position of pulmonary tuberculosis is lung and tuberculosis mycobacteria are infected in lung easily and repeatedly with a long development period and may easily cause bronchus blockage. And after a long period, the bronchus tissue may be damaged or dilated[5]. Generally, bronchial tuberculosis and pulmonary tuberculosis are in cross infection. Relevant studies mention that 40% ~ 90% active pulmonary tuberculosis patients are also troubled with bronchial tuberculosis. In a shorter period, bronchial tuberculosis may result in injury to bronchial cartilage and trachea, causing tracheal blockage, repeated pulmonary infection and even pulmonary tissue injury and afunction[6-8], and further resulting in great injury to human body. In addition, pulmonary tuberculosis may reoccur easily and produces resistance to pressure. At present, active pulmonary tuberculosis people are as high as 5 million and pulmonary tuberculosis has become one of the most difficult diseases in tuberculosis in China.

Different tuberculosis mycobacteria may cause different cell transformation, death and so on in different hosts. Interleukin -1p (IL-1p) is an inflammatory factor related to inductive cell death and can boost up and promote the activity of a protein Caspase1 related to apoptosis. The tumor necrosis factor (TNF-α) has no influence on normal cells but can kill cancer cells in patient's body. After the human body is infected with tuberculosis mycobacteria, an amount of IL-1p and TNF-α is helpful to recover bronchial and pulmonary tuberculosis. But, when IL-1p and TNF-α concentrations are too high, the state of the illness may be aggravated and normal immune system of the human body may be affected as well.

Relevant reports also mention that the infectiveness of tuberculosis mycobacteria is related with TNF-α concentration in patients' bodies to certain extent: the higher the concentration is and the higher the infected tuberculosis mycobacteria concentration is, the more serious the illness becomes[9]. Some studies indicate that IL series possibly play a very important role in occurrence and development of infectious diseases[10-11]. Meanwhile, IL involves in operation of human immune system. IL-1p can promote macrophages to phagocytize and kill tubercle bacteria. In addition, IL-1p can stimulate and bring TNF-α into play in antitubercular immune system[12-13]. Sometime, IL-1p and TNF-α may promote occurrence of the disease in abnormal circumstances. IFN-γ-inducible protein 10 (IP-10) is a chemotactic factor induced by lipopolysaccharide or IFN-γ and can promote and activate lymphocytes in inflammatory tissues[14].

After a patient is infected with bronchial or pulmonary tuberculosis, IP-10 may cause a number of monocytes and T cells to assemble in the infected positions, finally causing occurrence of diseases. Monocyte chemoattractant protein-1 (MCP-1) and macrophageinflammatoryprotein-1p (MIP-1p) have similar functions as IP-10 in human bodies. After bronchus or lung is infected with tuberculosis mycobacteria and suffers from inflammation, chemotactic factors MCP-1, MIP-1p and IP-10 are released to further promote the occurrence of the disease and regulate relevant effector cells[15]. Moreover, regulatory T cells and T-cell lymph groups produce protective immunity reaction by regulating the body and promote the generation of inflammatory factors IL-1p, TNF-α and so on to realize antituberculous immunity[16-17].

Some studies indicate that pulmonary tuberculosis patients resist and kill tuberculosis mycobacteria through internal IL-1p and TNF-α and also stimulate inflammatory reaction of pulmonary tissue[3]. Some studies have found that tuberculosis mycobacteria can stimulate a number of IP-10 and MCP-1 in the body of the pulmonary tuberculosis patient and joint inspection of IP-10, MCP-1 and other factors can improve the sensitivity of tuberculosis mycobacteria[18]. Pan Yanyu, et al.[19] also confirms this viewpoint in their study and soluble IL-2, membrane IL-2, IFN-γ, TNF-α and IP-10 are significantly different in tuberculosis patients and other people[20]. In the study of Yu Haibo, et al[21], it is also discovered that MCP-1 content obviously rises up in pulmonary tuberculosis patients while compared with the healthy people.

In this study, all indicators of bronchial and pulmonary tuberculosis patients are substantially close and also higher than the healthy people, which is identical to the result of the previous study. In addition, IL-1p, TNF-α, IP-10, MCP-1 and MIP-1p have identical changing tendency in bronchial and pulmonary tuberculosis patients and their concentrations may reflect the infection degree of the patient. In conclusion, IL-1p, TNF-α, IP-10, MCP-1 and MIP-1p reflect the infection conditions of bronchial and pulmonary tuberculosis patients during the infection of tuberculosis mycobacteria to certain extent, can be used as assistant indicators for diagnosing bronchial tuberculosis and pulmonary tuberculosis so as to win the best treatment period for patients, and can also be used as a testing indicator for patients in the process of treatment.

Meanwhile, this testing method is simple and quick, does not cause other injuries to the patients and can be promoted and applied widely.

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