Detection and significance of serum interleukin-6, tumor necrosis factor-α and interleukin-1β in first-episode schizophrenia patients

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Objective: To detect changes of serum interleukin-6, tumor necrosis factor-α and interleukin-1β in first-episode and different subtypes, and to analyze the correlation between pathological and immune mechanism.

Methods: 90 first-episode schizophrenia patients admitted to our hospital were enrolled as observation group, and were subdivided into four groups including negative and positive, family type and distributing types. During the same period, 35 physical healthy volunteers were enrolled as control group. Serum interleukin-6, tumor necrosis factor-α and interleukin-1β in both observation group and control group were detected with enzyme-linked immunosorbent (ELISA), correlation between these factors and mental symptoms were analyzed with pearson correlation analysis.

Results: The levels of serum IL-6, TNF-α, IL-1β of the observation group before and after the treatment were significantly higher than those of control group, the level of IL-1β in observation group after treatment was significantly lower than that before the treatment (P<0.05). Before treatment, the level of IL-6 in family type was significantly higher than that in distributing type, the level of TNF-α in negative type was significantly higher than that in positive type. After treatment the level of TNF-α was significantly reduced in family type and negative type, the IL-1β was significantly reduced in four subtypes. Pearson correlation analysis showed that TNF-α level was positively correlated with symptoms of negative subtype. IL-1β level and PANSS scores, symptoms of both positive and negative types were positively correlated.

Conclusion: The levels of IL-6, TNF-α, IL-1β levels are significantly increases in patients with first-episode schizophrenia, immune activation may be activated and IL-6 level is closely related to the family type of the disease which is genetic influenced, TNF-α is associated with symptoms of negative type. IL-1β level may be a certain extent reflecting the remission of the disease.

1. Introduction

Schizophrenia is a clinically common severe psychosis. Currently, its pathogenesis is unclear. Studies have pointed out that central dopamine nervous system disorders and immune mechanisms in addition to genetic and environmental influences may be involved in its occurrence and development[1,2]. Cytokines are important molecules for information exchange between the endocrine system, nervous system and immune system. They regulate nervous system and affect the balance between neuropeptides and neurotransmitters[3,4]. This study examined serum levels of interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) and interleukin change-1β (IL-1β) in 90 cases of first-episode schizophrenia patients with different subtypes and also analyzed the relevance between spirit pathology and immune mechanisms.

2. Materials and methods

2.1. General information

A total of 90 cases admitted to our hospital between February 2013 and August 2014 were enrolled and classified into observation group. All patients met the diagnostic criteria for schizophrenia[5] and were attacked for the first time with courses of less than 2 years. All patients did not take any antipsychotics. Pregnant and lactating...
women, patients with severe heart and kidney disease, malnutrition, immune system, endocrine system and other mental disorders, and patients receiving immunotherapy and hormone therapy were excluded. Of the 90 patients, 60 were male and 30 were female, with age ranging from 22 to 44 years [mean age of (31.36±12.92) years]. Clinical data of the patients were collected and scored using the Positive and Negative Syndrome Scale (PANSS) with 16 general psychopathology scales, 7 positive scales and 7 negative scales. According to the difference between the positive scales and negative scales, the patients were divided into two subtypes, negative and positive. There are 36 cases with less than 0 negative subtype minus points and 54 cases with greater than 0 positive subtype minus points. The patients were also divided into 39 cases of familial type and 51 cases of sporadic type. Thirty-five healthy volunteers [25 males and 10 females, age range of 23 to 50 years, and mean age of (33.10±13.24) years] who visited our hospital for physical examination during the same period were selected as control. No statistically significant difference in age and gender was found between the observation group and control group.

2.2. Treatment

After exact diagnosis, the patients in the observation group were given risperidone with an increasing dose from 1 to 6 mg/d. Two weeks later, a constant dose was used for the following 2 months. During the treatment period, artane and sedative-hypnotic drugs of benzodiazepine class were used to treat extrapyramidal reactions and poor sleep respectively, if needed.

2.3. Observed indicators

To detect serum levels of IL-6, TNF-α and IL-1β before and after the treatment, 3-5 mL fasting venous blood was taken from elbows of the control group before the treatment and from those of the observation group before and after the treatment. Serum was separated by centrifugation and saved at -20 °C for use. The serum levels of IL-6, TNF-α and IL-1β were detected using enzyme-linked immunosorbent assay (ELISA) kits (Kinbio Tech, Shanghai, China) in accordance with the manufacture instructions.

2.4. Statistical analysis

Statistical analysis was performed using SPSS 17.0. The measurement data are expressed as mean ± standard deviation and were analyzed using the t test. Correlation was analyzed using Pearson correlation analysis. P<0.05 was considered for statistically significant differences.

3. Results

3.1. Comparison on serum levels of IL-6, TNF-α and IL-1β before and after treatment

The serum levels of IL-6, TNF-α and IL-1β were significantly higher in the observation group than in the control group before the treatment (P<0.05). The level of IL-1β was significantly lower after the treatment than that before the treatment in the observation group (P<0.05). However, the treatment did not lead to statistically significant changes in the levels of IL-6 and TNF-α in the observation group (Table 1).

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Time</th>
<th>IL-6 (pg/mL)</th>
<th>TNF-α (pg/mL)</th>
<th>IL-1β (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>90</td>
<td>Before</td>
<td>20.43±7.22*</td>
<td>34.75±8.10*</td>
<td>25.45±5.64*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>20.12±7.15*</td>
<td>33.31±7.65*</td>
<td>18.80±4.67*#</td>
</tr>
<tr>
<td>Control group</td>
<td>35</td>
<td>Before</td>
<td>15.96±6.83</td>
<td>18.38±5.94</td>
<td>12.12±2.87</td>
</tr>
</tbody>
</table>

*P<0.05 vs the control group; #P<0.05 vs the observation group before the treatment.

3.2. Comparison on serum levels of IL-6, TNF-α and IL-1β in different subtypes before and after treatment

Before the treatment, the level of TNF-α was significantly higher than in the negative subtype patients than in the positive subtype ones (P<0.05), and the level of IL-6 was significantly higher than in the familial type patient than in the sporadic type ones (P<0.05). After the treatment, the levels of TNF-α was significantly decreased in the negative subtype patients and familial type patients compared with that before the treatment (P<0.05), and the level of IL-1β was found to significantly decrease in all patients (P<0.05) (Table 2).

<table>
<thead>
<tr>
<th>Subtype</th>
<th>n</th>
<th>Time</th>
<th>IL-6 (pg/mL)</th>
<th>TNF-α (pg/mL)</th>
<th>IL-1β (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>36</td>
<td>Before</td>
<td>21.09±7.13</td>
<td>38.65±9.96#</td>
<td>25.14±5.43</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>19.67±7.87</td>
<td>34.67±8.23&amp;</td>
<td>17.69±4.86&amp;</td>
</tr>
<tr>
<td>Negative</td>
<td>54</td>
<td>Before</td>
<td>22.12±7.43</td>
<td>30.27±7.65</td>
<td>25.97±5.97</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>22.32±7.65</td>
<td>30.08±8.54</td>
<td>18.99±4.43&amp;</td>
</tr>
<tr>
<td>Familial</td>
<td>39</td>
<td>Before</td>
<td>25.86±7.13#</td>
<td>35.16±9.22</td>
<td>25.28±5.64</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>25.13±7.63</td>
<td>32.65±7.94&amp;</td>
<td>17.96±4.28&amp;</td>
</tr>
<tr>
<td>Sporadic</td>
<td>51</td>
<td>Before</td>
<td>18.24±5.16</td>
<td>33.38±7.62</td>
<td>25.88±5.75</td>
</tr>
<tr>
<td></td>
<td></td>
<td>treatment</td>
<td>17.83±6.84</td>
<td>33.69±8.12</td>
<td>19.25±4.64#</td>
</tr>
</tbody>
</table>

*P<0.05 vs the positive subtype patients before the treatment; #P<0.05 vs the sporadic type patients before the treatment; &P<0.05 vs that before the treatment.

3.3. Correlation between the PANSS scores and levels of IL-6, TNF-α and IL-1β in the observation group before the treatment

Pearson correlation analysis showed that the TNF-α level was...
positively correlated with points for negative symptoms, and the IL-1β level was positively correlated with PANSS total score, points for negative symptoms, and points for negative symptoms (Table 3).

Table 3
Correlation between the PANSS scores and levels of IL-6, TNF-α and IL-1β.

<table>
<thead>
<tr>
<th>Factors</th>
<th>IL-6</th>
<th>TNF-α</th>
<th>IL-1β</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P</td>
<td>r</td>
</tr>
<tr>
<td>PANSS total score</td>
<td>0.018</td>
<td>0.786</td>
<td>0.089</td>
</tr>
<tr>
<td>Points for positive symptoms</td>
<td>0.095</td>
<td>0.328</td>
<td>0.023</td>
</tr>
<tr>
<td>Points for negative symptoms</td>
<td>0.044</td>
<td>0.657</td>
<td>0.554</td>
</tr>
</tbody>
</table>

4. Discussion

Schizophrenia is a common clinical psychoses, patients of which often suffer from perception, thinking, behavior and emotional disorders as well as uncoordinated mental activities[6]. The disease usually occurs with subacute or slow onset in young persons. The patients usually have clear consciousness and normal intelligence, but cognitive function will be damaged with the development of the disease. In addition, the disease is often recurrent. These bad factors have brought serious effects on the patient’s body and mind as well as the family and society[7,8]. To explore the etiology and pathogenesis of schizophrenia has always been a hot topic of research in psychiatry.

Currently, the pathogenesis of schizophrenia is not yet clear. Studies have pointed out that central dopamine nervous system disorders and immune mechanisms in addition to genetic and environmental influences may be involved in the development and progression of the disease[1,2]. Cytokines are important molecules for information exchange between the endocrine system, nervous system and immune system. They regulate nervous system and affect the balance between neuropeptides and neurotransmitters[3,4]. Cytokine-mediated immune dysfunction may happen in schizophrenia patient, thus breaking the balance between the endocrine system, nervous system and immune system and also causing abnormal secretion of neurotransmitters which are involved in the pathophysiology of psychiatric disorders[9,10].

In this study, the expression of three kinds of cytokines (IL-6, TNF-α and IL-1β) was detected in the first episode schizophrenia patients. Compared with the healthy volunteers, these patients had significantly higher serum levels of IL-6, TNF-α and IL-1β before and after the treatment (P<0.05), suggesting the presence of immune activation and cytokine involvement in schizophrenia patients. Additionally, the level of IL-6 was significantly higher in the familial type patients than in the sporadic type ones (P<0.05), revealing that IL-6 is closely related to the family type. Genetic predisposition is often present most of schizophrenia patients. Compared with sporadic type patients, familial type patients have more obvious genetic characteristics; thus, genetic background may influence serum IL-6-mediated immune function[11,12]. We also found the level of TNF-α was significantly higher in the negative subtype patients than in the negative subtype ones (P<0.05), and the level of TNF-α in the positive subtype and familial type patients was significantly after the treatment than that before the treatment (P<0.05). These results showed that TNF-α is related with improvement of negative symptoms. The TNF-α level was positively correlated with points for negative symptoms, and familial type negative schizophrenia patients usually show negative symptoms; therefore, the TNF-α level also significantly reduced after the treatment[13,14]. Some studies demonstrate that the secretion of cytokines is also affected by antipsychotics drugs in addition to the basic effect. They showed that antipsychotics can relieve symptoms in schizophrenic patients and reverse cytokine-mediated immune abnormalities[15]. Thus, to choose cytokines is of significance for the prediction and assessment of therapeutic effect of the disease. Our study showed that the serum level of IL-1β was decreased in all patients and it was positively correlated with PANSS total score, points for positive symptoms and points for negative symptoms. These results revealed the IL-1β is related with psychiatric symptoms in schizophrenia patients and can reflect alleviation of the disease to a certain degree, maybe because IL-1β affects neurotransmitters, especially catecholaminergic.

In summary, the results of the study showed that first-episode schizophrenia patients had significantly higher serum levels of IL-6, TNF-α and IL-1β. Immune activation may happen in the patients. IL-6 is closely related to familial genetic effects, TNF-α is related with negative symptoms and improvement, and IL-1β reflects alleviation of the disease to a certain degree. Due to limited experimental conditions, this study failed to further explain how the immune system affects psychopathology at a gene level, which needs further researches.

References


[16] Song XQ, Chen XM, Zhang W. Study of adiponectin, IL-1β, IL-6 and TNF-α in first episode drug naïve schizophrenia. *Zhonghua Yi Xue Za Zhi* 2013; 93(41): 3256-60.