



Relationship of serum neurotransmitters with anxiety depression, T lymphocyte subsets and NK cells in patients with lung cancer chemotherapy

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ABSTRACT

Objective: To study the relationship of serum neurotransmitters with anxiety depression, T lymphocyte subsets and NK cells in patients with lung cancer chemotherapy. **Methods:** 56 cases of patients with advanced lung cancer who received chemotherapy in the First Affiliated Hospital of Chengdu Medical College between July 2013 and August 2016 were collected as observation group, and 50 healthy subjects who received physical examination in our hospital during the same period were selected as normal control group. Serum neurotransmitter, negative emotions and immune index levels were compared between the two groups of subjects. Pearson test was used to evaluate the relationship of serum neurotransmitter contents with negative emotions and immune index levels in patients with lung cancer chemotherapy. **Results:** Serum neurotransmitters DA, 5-HT and NE contents in observation group were lower than those in normal control group; SAS and SDS scores were higher than those of normal control group; peripheral blood CD4⁺T lymphocyte level, CD4⁺/CD8⁺ ratio and NK cell level were lower than those in normal control group while CD8⁺T lymphocyte level was higher than that in normal control group. Pearson test showed that serum neurotransmitters DA, 5-HT and NE contents in patients with lung cancer chemotherapy were directly correlated with anxiety depression, T lymphocyte subset and NK cell levels. **Conclusion:** Serum neurotransmitter expression decrease in patients with lung cancer chemotherapy, and this is one of the important causes of anxiety depression and immune dysfunction in patients.

1. Introduction

Chemotherapy is the main treatment of lung cancer late, but many studies have found that the probability of emotional disorders dramatically increases after systemic chemotherapy, and immune dysfunction easily appear[1,2]. It was believed that both unhealthy emotions and immunosuppressive state in patients with advanced cancer chemotherapy are caused by the side effects of chemotherapy drugs, but with the deepening of the clinical research, more and

more scholars believe that in addition to drug effect, they may be closely related to the abnormal neurotransmitter levels. Monoamine neurotransmitter hypothesis is the key of study on depression prevention and treatment accepted at present, and its expression reduction can directly increase the incidence of depression in rats, and further affect the body's immune function through nerve-immunity mechanism[3,4]. At present, there is not much study on the neurotransmitter expression changes in patients with chemotherapy, serum levels of neurotransmitters were compared between patients with lung cancer chemotherapy and normal subjects in the study, and the inner link of their expression changes with patients' negative mood and immune state was further explored, now reported as follows.

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2. Information and methods

2.1 General information

56 cases of patients with advanced lung cancer who received chemotherapy in the First Affiliated Hospital of Chengdu Medical College between July 2013 and August 2016 were collected as observation group, 50 healthy subjects who received physical examination in our hospital during the same period were selected as normal control group, and two groups of subjects themselves signed informed consent. Observation group included 30 men and 26 women that were 34-71 years old; control group included 26 men and 24 women that were 32-70 years old. The gender and age distribution were not statistically different between the two groups ($P>0.05$), and the study was approved by the hospital ethics committee.

Inclusion criteria: (1) without history of emotional disorders such as anxiety or depression; (2) with normal nerve function, and without history of stroke/cerebral infarction, or brain trauma; (3) cooperating with the whole inspection and with complete data. Exclusion criteria: (1) associated with severe autoimmune diseases; (2) associated with systemic infectious diseases.

2.2 Serum neurotransmitters

2.0 mL fasting cubital venous blood was extracted from observation group after chemotherapy and from normal control group immediately after inclusion, the blood was anti-coagulated and centrifuged at low speed to obtain the upper serum, and the enzyme-linked immunosorbent assay (ELISA) was used to determine the levels of neurotransmitters in it, including dopamine (DA), 5-hydroxytryptamine (5-HT) and norepinephrine (NE).

2.3 Anxiety depression

Self-rating anxiety scale (SAS) organized by Zung was used to evaluate the degree of depression of observation group after chemotherapy and of normal control group immediately after inclusion, the score was 20-80 points, and the higher the score, the severer the anxiety; self-rating depression scale (SDS) organized by Zung was used to assess the extent of depression of both groups of subjects, the score was 20-80 points, and the higher the score, the severer the depression.

2.4 T lymphocyte subsets and NK cells

2.0 mL fasting cubital venous blood was extracted from observation group after chemotherapy and from normal control group immediately after inclusion in the same way, flow cytometer (BD Biosciences in US, model BD FACSCanto II) was used to detect the levels of T lymphocyte subset cells CD4⁺ and CD8⁺, CD4⁺/CD8⁺ ratio was calculated, and the NK cell levels were also determined.

2.5 Statistical processing

Data were recorded and calculated by the professionals, and statistical software was SPSS 21.0. Neurotransmitters, negative emotion score, immune function indexes and other measurement data were in terms of mean \pm standard deviation ($\bar{x}\pm s$), and comparison between two groups was by grouping t test. Statistics $P<0.05$ in the study was the standard of statistical significance in differences.

3. Results

3.1 Neurotransmitters

Comparison of serum neurotransmitters DA (ng/L), 5-HT ($\mu\text{g/L}$) and NE (ng/L) contents between two groups of research subjects was as follows: serum DA, 5-HT and NE contents in observation group were significantly lower than those in normal control group. Differences in serum neurotransmitters DA, 5-HT and NE contents were statistically significant between two groups of research subjects ($P<0.05$), shown in Table 1.

Table 1.

Comparison of serum neurotransmitter contents between two groups of research subjects.

Groups	<i>n</i>	DA	5-HT	NE
Normal control group	50	69.75 \pm 8.23	0.92 \pm 0.11	41.86 \pm 5.37
Observation group	56	36.48 \pm 4.51	0.59 \pm 0.07	29.74 \pm 3.42
<i>t</i>		18.291	6.382	14.207
<i>P</i>		<0.05	<0.05	<0.05

3.2 Anxiety depression

SAS score of normal control group was (25.48 \pm 3.96) points, and SDS score was (27.17 \pm 4.28) points; SAS score of observation group was (59.62 \pm 8.15) points, and SDS score was (62.63 \pm 8.49) points. SAS and SDS scores of observation group were significantly higher than those of normal control group, and differences in SAS and SDS scores were statistically significant between two groups of research subjects ($P<0.05$).

3.3 T lymphocyte subsets and NK cells

Comparison of peripheral blood CD4⁺ and CD8⁺T lymphocyte levels, CD4⁺/CD8⁺ ratio and NK cell levels between two groups of research subjects was as follows: peripheral blood CD4⁺T lymphocyte level, CD4⁺/CD8⁺ ratio and NK cell level in observation group were significantly lower than those in normal control group while CD8⁺ T lymphocyte level was higher than that in normal

control group. Differences in peripheral blood CD4⁺ and CD8⁺T lymphocyte levels, CD4⁺/CD8⁺ ratio and NK cell levels were statistically significant between two groups of research subjects ($P < 0.05$), shown in Table 2.

Table 2.

Comparison of peripheral blood T lymphocyte subset and NK cell levels between two groups of research subjects.

Groups	n	CD4 ⁺	CD8 ⁺	CD4 ⁺ /CD8 ⁺	NK
Normal control group	50	49.23±5.61	18.62±2.19	2.27±0.34	31.62±4.04
Observation group	56	38.76±4.07	27.34±3.11	1.56±0.24	18.23±2.51
<i>t</i>		14.381	11.624	6.301	13.274
<i>P</i>		<0.05	<0.05	<0.05	<0.05

3.4 Correlation analysis

Pearson test showed that serum neurotransmitters DA, 5-HT and NE contents in patients with lung cancer chemotherapy were negatively correlated with SAS and SDS scores; they were positively correlated with T lymphocyte subset CD4⁺T lymphocyte level and CD4⁺/CD8⁺ ratio, negatively correlated with CD8⁺T lymphocyte level and positively correlated with NK cell level ($P < 0.05$), shown in Table 3.

4. Discussion

Patients with advanced lung cancer are generally anxious and depressed after chemotherapy, and they are also complicated with immune function weakening, which is bad for their recovery. Previous studies believe that the bad mood and weakened immune function in patients with advanced cancer mainly come from their worries about treatment outcome and toxic side effect injury during chemotherapy, but the latest studies suggest that the neurotransmitter expression change is also involved[5,6]. DA, 5-HT and NE are the most typical monoamine neurotransmitters synthesized and secreted by sympathetic postganglionic neurons and intracerebral adrenergic nerve endings, and DA not only plays the physiological role in regulating extrapyramidal system, but also has certain anti-tumor feature; 5-HT and NE are the essential substances that maintain normal emotional state of the body, and the reduction of

their expression can lead to emotional excitability decrease and depression[7,8]. In the study, serum contents of DA, 5-HT, NE and other monoamine neurotransmitters were compared between two groups of subjects, and it was found that compared with normal control group, the observation group of patients were with lower serum contents of DA, 5-HT and NE, confirming that the expression of monoamine neurotransmitters decrease in patients with lung cancer after chemotherapy, and the inner link of the phenomenon with negative emotions and immune state remains to be confirmed in following study.

There are common negative emotions such as anxiety and depression in patients with advanced cancer, which can directly affect their treatment compliance and ultimately determine the treatment outcome to a great extent[9,10]. SAS and SDS are the most common clinical scales to determine the negative emotions of a patient, and their reliability and validity are both recognized[11]. In the study, negative emotion scores were compared between the two groups, and it was found that compared with normal control group, the observation group of patients were with higher SAS and SDS scores, which are anastomotic with the emotional characteristics of patients with cancer. Further Pearson test showed that serum neurotransmitters DA, 5-HT and NE contents in patients with lung cancer chemotherapy were negatively correlated with SAS and SDS scores, confirming that the decreased expression of monoamine neurotransmitters is directly correlated with the patient's negative emotions.

Immune status greatly determines the treatment outcome of patients with advanced cancer, and there is immunosuppressive state in the vast majority of patients after chemotherapy, which is speculated to be directly correlated with the toxic reactions of chemotherapy drugs[12,13], but there is no clear conclusion whether it is associated with neurotransmitter expression change. In the study, peripheral blood T lymphocyte and NK cell levels were compared between the two groups, and it was found that compared with normal control group, the observation group of patients were with lower peripheral blood CD4⁺T lymphocyte level, CD4⁺/CD8⁺ ratio and NK cell level, and higher CD8⁺ T lymphocyte level. Cellular immunity plays a decisive role in antitumor immunity, CD4⁺T lymphocytes are effector cells, and CD4⁺/CD8⁺ ratio directly reflects the body's

Table 3.

Correlation of serum neurotransmitters with negative emotions and immune function in patients with lung cancer chemotherapy

Indexes	DA		5-HT		NE	
	Determination coefficient r	P	Determination coefficient r	P	Determination coefficient r	P
SAS	-0.617	<0.05	-0.615	<0.05	-0.577	<0.05
SDS	-0.599	<0.05	-0.589	<0.05	-0.726	<0.05
CD4 ⁺	0.748	<0.05	0.726	<0.05	0.711	<0.05
CD8 ⁺	-0.625	<0.05	-0.649	<0.05	-0.673	<0.05
CD4 ⁺ /CD8 ⁺	0.692	<0.05	0.705	<0.05	0.712	<0.05
NK	0.721	<0.05	0.674	<0.05	0.583	<0.05

cellular immune function; NK cells are natural killer cells that can attack malignant tumor cells directly and weaken their activity[14-16]. These results show that there is obvious immunosuppression in patients with lung cancer, and further Pearson test showed that serum neurotransmitters DA, 5-HT and NE contents patients with lung cancer chemotherapy were positively correlated with peripheral blood T lymphocyte subset CD4⁺T lymphocyte level, CD4⁺/CD8⁺ ratio, and negatively correlated with CD8⁺ T lymphocyte level, confirming that the decreased expression of monoamine neurotransmitters can directly result in the decline of the body's immune function.

There is obviously decreased expression of monoamine neurotransmitters in patients with lung cancer chemotherapy, which can directly affect the anxiety depression and other negative emotions, and also inhibit the body's immune status. Intervening with the neurotransmitter expression is expected to become a new long-term adjuvant therapy for patients with advanced cancer and remains to be further explored in subsequent research.

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