Research Paper

Effects of Sertraline on T lymphocyte Subsets, Depression and Quality of Life in Lung Cancer Patients with Depression

XU LU, YINQIAO CHEN, X. W. XU AND P. Z. ZHU*

Department of Oncology, Yongkang First People's Hospital, Yongkang, Zhejiang 321300, China

To investigate the effects of sertraline on T lymphocyte subsets, depression and quality of life in lung cancer patients with depression is the objective of the study. A total of 100 lung cancer patients with depression admitted from January 2020 to June 2021 were randomly divided into two groups. The control group (50 cases) received conventional clinical pathway management and psychological treatment and the research group (50 cases) received treatment on the basis of the control group and combined with sertraline 50-200 mg/d. Both groups were observed for 6 w. T lymphocyte subsets and depression was compared before and after 3, 6 w of treatment, the quality of life was compared before and after 6 w of treatment. The adverse drug reactions were also recorded. In terms of T lymphocyte subsets, the cluster of differentiation 4^+/cluster of differentiation 8^+ of research group was higher than control group ($p<0.01$). After 6 w, those in the research group were higher than control group ($p<0.05$) and cluster of differentiation 8^+ was lower than control group ($p<0.01$). In terms of depression, the scores of self-rating depression scale and Hamilton depression scale in research group were lower than control group ($p<0.05$) where it decreased in both groups after 6 w ($p<0.05$), in which the scores in research group after 6 w were lower than those after 3 w ($p<0.01$). In terms of quality of life, the scores of physical function, emotional function, energy, mental health, social function and general health in the research group were higher than control group ($p<0.01$) and higher than those before treatment ($p<0.01$). In addition, there was no adverse drug reactions occurred during the period of treatment. Sertraline can improve the degree of depression, T lymphocyte subsets function and quality of life in lung cancer patients with depression and be worthy of further clinical promotion.

Key words: Sertraline, lung cancer, depression, T lymphocyte subsets, quality of life

Depressive symptoms are common in cancer patients after the diagnosis of the disease. Long-term depression can seriously affect patients quality of life and also cause mortality[1]. With the improvement of tumor treatment, clinicians should not only pay attention to the treatment of the disease itself and the improvement of some physical symptoms, but also carry out adequate and timely diagnosis and treatment for patients mental symptoms[2-4]. Drug therapy is the most commonly used treatment for depression. Sertraline, as a representative agent of selective 5-Hydroxytryptamine (5-HT) reuptake inhibitors, has become the preferred antidepressant for cancer depression comorbidities[5,6].

And simultaneously, a recent study have reported that the occurrence and development of depression in tumor patients is related to cellular immunity[7]. However, the effect of sertraline on immune function of patients with tumor depression has not been clearly reported. This study was to investigate the effects of sertraline on T lymphocyte subsets, depression and quality of life in lung cancer patients with depression.

MATERIALS AND METHODS

Clinical data:

All patients with lung cancer in the oncology department of Yongkang first people's hospital from January 2020 to June 2021 were studied. Inclusion criteria included 35~80 y old; pathological diagnosis as lung cancer; 72 scores>Self-rating Depression Scale (SDS)≥53 scores; or 35 scores>Hamilton Depression Scale (HAM-D) (24-item version)≥8 scores; expected survival≥6 mo; having the health-conscious and ability of language communication. Exclusion criteria included serious mental retardation or cognitive impairment; mental illness or serious heart disease, liver and kidney

***Address for correspondence**
E-mail: zhupeizhen668@163.com

dysfunction, infections; had received or been receiving the synchronous radiotherapy or chemotherapy within 1 mo; there are contraindications to drugs. Withdrawal criteria included serious adverse reactions, complications and special disease changes occurred during the study period; could not complete 6 cycles of treatment; patients or their family members wanted to withdraw. A total of 100 patients with lung cancer patients were enrolled and were divided into control group and research group by random number table. This study was reviewed and approved by Committee on Medical Ethics of Yongkang First People's Hospital (No. ykyy2020-04), and all patients signed the informed consent.

Patient characteristics:

General information of patients at baseline were recorded, including the gender, age, marital status, educational, monthly income, pathological type of lung cancer, clinical stage, etc.

Groups and interventions:

The control group was given treatment plan and drugs related to clinical pathway management, at the same time, psychological counseling was given by the hospital psychological consultants. The research group was given sertraline 50 mg (Jiangsu Hengrui Medicine Co., Ltd., specification: 60 mg/tablet, approval number: Guoyaozhunzi H20050899), once a day (q.d.), orally (p.o.) on the basis of the control group and simultaneously, the dose of sertraline should be adjusted once a week by the competent physician and a psychological consultant to judge the patient's depression and tolerance, and the maximum dose should not exceed 200 mg/d. Patients in both groups were observed for 6 w. T lymphocyte subsets, SDS[8], HAM-D (24-item version)[9] were evaluated at admission and after 3 and 6 weeks of treatment, the Medical Outcomes Study (MOS) 36-Item Short Form Health Survey (SF-36)[10] was used to assess patients quality of life at admission and after 6 w of treatment. Any Adverse Events (AEs) occurred during the study were recorded. In addition, all adverse drug reactions were recorded during the observation period.

Scoring criteria:

T lymphocyte subsets determination: Fasting elbow venous blood was taken from all patients in the morning and T lymphocyte subsets (Cluster of Differentiation (CD) 3^+, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$, Natural Killer (NK) cells) were determined by flow cytometry (BD, FACSCanto II). All tests were carried out strictly in accordance with kit instructions. Normal values: $CD3^+$: 53.89 %-75.31 %, $CD4^+$: 27 %-51 %, $CD8^+$: 15 %-44 %, $CD4^+/CD8^+$: 0.95 %-2.11 %, NK: 7 %-40 %.

SDS: There were 20 items in each scale. The sum of all items was a rough score, which was multiplied by 1.25 to get a standard score. A standard score of 50 was used as the boundary for depression.

HAM-D -24: There were 24 items in total and 10 items were scored according to three grades: None (0), mild to moderate (1), severe (2); Grade five (14): None (0), mild (1), moderate (2), severe (3), very severe (4). Normal: <8 points; mild depression: 8 to 20; moderate depression: 20 to 35; major depression: >35.

SF-36: Contains 8 dimensions and 36 entries. The score is converted by [(original score-lowest possible score)/ general average possible score×100] and the score range of each dimension is 0-100 points after conversion. The higher the score, the better the quality of life.

Statistical analysis:

All the data were statistically analyzed by excel and Statistical Package for the Social Sciences (SPSS) 17.0 software. Descriptive statistics were recorded as counting data and the measurement data were expressed as mean±standard deviation. Two independent samples t-test and paired t-test were used for comparison between groups of normally distributed data. Repeated measurement analysis of variance was used for the mean of multiple groups and Least Significant Difference (LSD) method was used for pairwise comparison among multiple groups. The comparison between groups of non-normal distribution data was conducted using rank sum test and the generalized estimation equation was used among multiple means. Chi-square test (bilateral) was performed for enumeration data, $p<0.05$ indicated that the difference was statistically significant.

RESULTS AND DISCUSSION

Through the comparative analysis of all the general information of enrolled patients, there was no statistically significant difference between the two groups in gender, age, marital status, educational, monthly income, pathological type of lung cancer and clinical stage ($p>0.05$) , as shown in Table 1.

TABLE 1: GENERAL INFORMATION AT BASELINE BETWEEN THE TWO GROUPS

Classification	Control group (n=50)	Research group (n=50)	t/χ^2	p
Age (years, $\bar{x}\pm s$)	58.86±9.55	59.51±9.87	0.456	0.649
Gender (n)			0.364	0.546
Male	29	26		
Female	21	24		
Marital status (n)			0.154	0.695
Married	46	47		
Unmarried	4	3		
Educational (n)			0.509	0.917
Primary school	18	19		
Junior high school	8	10		
Senior high school	14	13		
Graduate	10	8		
Monthly income (n)			1.129	0.569
≤4000 Yuan	13	17		
4000~8000 Yuan	25	20		
≥8000 Yuan	12	13		
Pathological (n)			1.103	0.576
Adenocarcinoma	34	29		
Squamous carcinoma	11	15		
Small cell lung cancer	5	6		
Clinical stage (n)			1.115	0.774
I	2	1		
II	11	8		
III	24	28		
IV	3	3		

Comparison of the T lymphocyte subsets in different periods between the two groups was determined here. There were no statistically significant differences in T lymphocyte subsets at baseline between the two groups (p>0.05). After 3 w of treatment, $CD4^+/CD8^+$ in the research group was significantly higher than that in control group (p<0.01). In addition, after 6 w, $CD4^+$ and $CD4^+/CD8^+$ in the research group were significantly higher than those in the control group (p<0.05). $CD8^+$ was significantly lower than control group (p<0.01). Meanwhile, results showed that after 2 w and 4 w treatment there was significant increase in $CD3^+$, $CD4^+/CD8^+$ in control group (F=5.453, 4.828, p<0.01). $CD3^+$ and $CD4^+/CD8^+$ increased significantly at 6 w compared with the status of admission (t=3.192, 3.075, p<0.05). However, the differences of T lymphocyte subsets in three periods were statistically significant (F=7.949, 7.635, 5.029, 23.528, 3.937, p<0.05). All indexes of T lymphocyte subsets were significantly improved at 6 w compared with those at admission (t=4.507, 4.133, 2.775, 6.648, 2.781, p<0.05). Compared with 3 w, $CD4^+/CD8^+$ increased more significantly at 6 w (t=1.433, p<0.05) as shown in Table 2.

Comparison of the scores of the depression in different periods between the two groups was shown here. There was no significant difference in SDS and HAM-D scale scores at baseline between the two groups (p>0.05). After 3 w and 6 w of treatment, SDS and HAM-D scores in the research group were significantly lower than those in the control group (p<0.05). Once after admission in the control group, depression conditions were improved after 3 w and 6 w of treatment (F=9.470, 8.660, p<0.05). In addition, SDS and HAM-D scores after 6 w were significantly higher than those at admission (t=4.545, 4.275, p<0.05). However, in the intervention group, depression conditions were also improved after 3 w and 6 w treatment (F=39.290, 37.720, p<0.01). Excitedly, during completion of the 3 w and 6 w of treatment, SDS and HAM-D scores were significantly reduced compared with the status of admission (t=3.723, 4.316, 10.046, 10.107, p<0.05) and that compared with 3 w, SDS and HAM-D scores decreased more significantly at 6 w (t=4.577, 3.806, p<0.05) as shown in Table 3.

Comparison of the score of the quality of life in different periods between the two groups was shown below. There was no significant difference in quality of life scale scores at baseline between the two groups ($p>0.05$). After 6 w of treatment, the scores of role emotional, vitality, mental health, social function and general health in the research group were significantly higher than those at admission ($t=2.905$, 2.510, 2.224, 2.065, 2.351, $p<0.05$). Excitedly, the scores of physical role, emotional role, vitality, mental health, social function and general health in the research group were also significantly higher than those in the control group ($p<0.01$) was shown in Table 4.

The occurrence of adverse drug reactions was explained here. This study excluded the complications caused by non-sertraline drugs. During the process of treatment, there was no incidence of adverse drugs reactions in the research group.

After the occurrence of cancer, the prognosis of tumor, medical expenses, family life and public opinion are all risk factors for patients mood disorders[11-13]. In this study, patients in both groups were assessed as moderately depressed according to SDS and HAM-D at admission. After treatment with different methods, depression was improved in both groups ($p<0.05$), but the effect was more obvious in the research group ($p<0.05$). Analysis of the reasons, non-drug therapy (psychological therapy) can improve patient's depression, but it can't be well quantified and its operability varies from person to person. And at the same time, because of the heavy clinical workload of medical workers, psychological counseling alone cannot be effectively popularized. Therefore, not all patients have clinical benefits. Sertraline can significantly improve the depression of patients by highly selective inhibition of 5-HT reuptake and recovery, increasing 5-HT concentration in central nervous system and exerting antidepressant pharmacological activities[14,15].

In our study, the patient's depression improved continuously after 3 w to 6 w of treatment. However, they are still in mild depression, this suggests that patients with cancer and depression need long-term sertraline therapy. In addition, emotional function, vitality, mental health, social function and general health were also improved in the research group. Li XJ *et al.*[16] found that sertraline was also found to improve quality of life and executive function in patients with cancer and depression.

In terms of immune function, some studies have found that the immune function of tumor patients is inversely related to the level of depression[17,18]. With the increase of depression, T cell proliferation and activation were further inhibited, and the cell activity decreases[19-21]. Dai *et al.*[22] research found that before treatment, the NK cells, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ ratios of tumor patients decreased significantly, while $CD8^+$ increased. After 6 w of treatment, NK cells, $CD3^+$, $CD4^+$, $CD4^+/CD8^+$ ratios increased significantly and $CD8^+$ decreased. If depression can be detected in the early stage and antidepressant can be used, it can improve the depression situation and immune function of patients with malignant tumor. In this study, all indexes of T lymphocyte subsets of patients in the research group were significantly improved after treatment ($p<0.05$). These results indicated that sertraline not only improved the depressive state of patients, but also had a good regulation effect on T lymphocyte subsets. It can induce the increase of $CD4^+$ synthesis and differentiation, enhance the activity of patients T cells, and increase their ability to recognize and monitor antigens in contact with abnormal cells, and reduce the number of $CD8^+$, leading to the reduction of immunosuppressive factors. Moreover, the number of NK cells increases and cytotoxic factors are secreted to produce a powerful killing effect on abnormal cells, then preventing the spread of tumors. As the same with Pietruczuk *et al.*[23] research report that after 6 w of sertraline treatment, compared with before treatment, the levels of $CD3^+$, $CD4^+$ cells and $CD4^+/CD8^+$ in peripheral blood of patients with depression were significantly increased while the ratio of $CD8^+$ lymphocytes was significantly decreased ($p<0.01$).

In conclusion, lung cancer patients with depression have obvious immunosuppression, which should be paid enough attention in clinical diagnosis and treatment. Sertraline not only alleviates depression but also improves T lymphocyte subsets function and quality of life in these patients. In addition, there were no drug related adverse reactions in this study, which is of high safety and worthy of clinical application.

However, due to the limitations of time and manpower, the sample size of this study was relatively small and only T lymphocyte subsets were considered for immune function, so the observed indexes were not sufficient. In the future clinical practice, more sample sizes and indicators reflecting immune function status will be included. Moreover, a longer period of intervention and follow-up were also needed.

TABLE 2: COMPARISION OF THE T LYMPHOCYTE SUBSETS IN DIFFERENT PERIODS BETWEEN THE TWO GROUPS (x̄±s)

Periods	Group	$CD3^+$ (%)	$CD4^+$ (%)	$CD8^+$ (%)	$CD4^+/CD8^+$	NK (%)
At admission	Control	58.46±7.87	29.24±6.48	29.49±4.67	1.03±0.30	17.22±4.10
	Research	59.26±7.61	30.40±6.61	28.44±4.13	1.06±0.31	16.84±4.38
	t	0.519	0.886	1.191	0.42	0.448
	p	0.605	0.378	0.237	0.676	0.655
3 w treatment	Control	60.86±8.05	31.49±7.13	28.60±5.72	1.10±0.38	17.98±5.24
	Research	62.68±8.44	34.01±9.80	27.06±4.05	1.31±0.40^{aa}	18.42±4.92
	t	1.103	1.469	1.557	2.685	0.433
	p	0.273	0.145	0.123	0.009	0.666
6 w treatment	Control	63.54±7.30^{bb}	32.63±7.40	28.58±5.38	1.28±0.44^{b}	18.24±4.35
	Research	65.64±5.85^{bb}	35.99±7.59^{abb}	25.79±4.43^{aab}	1.53±0.36^{aabbc}	19.46±4.85b
	t	1.584	2.241	2.835	3.143	1.806
	p	0.116	0.027	0.006	0.002	0.074

Note: Compared with the control group at the same periods, $^{a}p<0.05$ and $^{aa}p<0.01$; compared with the same group at admission, $^{b}p<0.05$ and $^{bb}p<0.01$ and compared with the same group after 6 w, $^{c}p<0.05$

TABLE 3: COMPARISION OF THE SCORE OF SDS AND HAM-D IN DIFFERENT PERIODS BETWEEN THE TWO GROUPS (x̄±s)

Periods	Group	SDS	HAM-D
At admission	Control	68.22±3.28	29.54±4.30
	Research	68.02±3.17	29.98±5.51
	t	0.310	0.446
	p	0.757	0.657
3 w treatment	Control	66.82±4.28	26.84±5.26
	Research	64.46±5.71^{abb}	24.08±5.88^{abb}
	t	2.337	2.474
	p	0.021	0.015
6 w treatment	Control	65.12±4.42^{bb}	25.56±5.03b
	Research	59.26±6.77^{aabbcc}	19.60±4.76^{aabbcc}
	t	5.122	6.085
	p	0.000	0.000

Note: Compared with the control group at the same periods, $^{a}p<0.05$ and $^{aa}p<0.01$; compared with the same group at admission, $^{b}p<0.05$ and $^{bb}p<0.01$; compared with the same group after 6 w, $^{cc}p<0.05$

TABLE 4: COMPARISION OF THE SCORE OF THE QUALITY OF LIFE IN DIFFERENT PERIODS BETWEEN THE TWO GROUPS (x̄±s)

Periods	Group	Physiological function	Physical role	Emotional role	Vitality	Mental health	Social function	Bodily pain	General health
At admission	Control	60.08±9.59	62.66±12.13	60.90±8.67	60.64±10.91	59.96±9.47	63.62±10.58	61.92±9.89	65.50±11.89
	Research	60.46±8.85	62.94±8.67	62.66±9.02	61.32±10.83	59.98±10.79	62.98±11.25	62.34±8.56	66.30±8.72
t		1.043	1.216	0.775	0.964	1.564	1.004	0.877	1.407
p		0.302	0.23	0.442	0.34	0.124	0.32	0.385	0.166
6 w treatment	Control	61.02±8.70	63.78±11.90	61.64±8.42	61.62±10.44	61.72±9.48	64.56±10.28	62.94±8.85	66.88±9.88
	Research	62.14±8.22	66.04±9.08^{aa}	66.82±9.38^{aabb}	66.22±7.68^{aab}	65.52±7.49^{aab}	68.36±7.98^{aab}	64.04±9.47	71.02±7.58^{aab}
t		1.321	3.223	3.885	3.403	4.146	3.841	1.38	4.017
p		0.193	0.002	0	0.001	0	0	0.174	0

Note: Compared with the control group at the same periods, $^{aa}p<0.01$; compared with the same group at admission, $^{b}p<0.05$ and $^{bb}p<0.01$

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Xiangwei Xu and Peizheng Zhu contributed equally to this work. Conception and design of the research was done by Peizhen Zhu, Xiangwei Xu; acquisition of data: Yinqiao Chen, Lu Xu; analysis and interpretation of data: Xiangwei Xu; statistical analysis: Xiangwei Xu; drafting the manuscript: Peizhen Zhu; revision of manuscript for important intellectual content: Peizhen Zhu. All authors read and approved the final manuscript.

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Conflict of interests:

The authors declared no conflict of interest.

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