Study of prevalence and influencing factors of depression in tumor patients and the therapeutic effects of fluoxetine

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Abstract. - OBJECTIVE: To observe the depression in patients with malignant tumor and influencing factors of the disease, as well as to investigate the effects of fluoxetine on depressive symptoms in cancer patients and the immune function.

PATIENTS AND METHODS: 262 patients with malignant tumors, confirmed by pathological and radiological diagnosis as malignant tumor were randomly divided into 2 groups: the control group with chemotherapy; the treatment group with chemotherapy and 20 mg/d fluoxetine for six weeks. Before and after treatment, the scores of QLQ-C30 scale and changes of immune parameters were observed, including the determination of NK and T cell subsets.

RESULTS: The prevalence of depression in cancer patients was not related to the tumor location. But gender, age, tumor stage, the income level of satisfaction and chronic cancer pain were related to the occurrence of depression in cancer patients (p < 0.05). In the fluoxetine treatment groups, by QLQ-C30 scores, in quality of life scores including body, function, social and cognitive function, and single symptoms including nausea, vomiting, constipation, diarrhea, and economic difficulties, the differences were not statistically significant. The QLQ-C30 scores of overall quality of life and emotional function were rising in the fluoxetine treatment group. The QLQ-C30 scores of the pain, shortness of breath, fatigue, loss of appetite, insomnia symptoms were decreased, which had a statistical significance (p < 0.05) compared with the control group. To compare with the control group, the scores of HAMD were decreasing in the fluoxetine treatment group, which had a statistical significance (p < 0.05). Before treatment, the NK cells, CD3+, CD4+, CD4+/CD8+ ratios of tumor patients decreased significantly, while CD8+ increased. After 6 weeks of treatment, NK cells, CD3+, CD4+, CD4+/CD8+ ratios increased significantly and CD8+ decreased.

CONCLUSIONS: Sex, age, tumor stage, income satisfaction, and cancer pain were relevant factors in patients with tumor-associated depression. If depression can be detected in the early stage, and oral fluoxetine therapy can be conducted, it can improve the depression situation and immune function of patients with malignant tumor.

Key Words: Malignant tumor, Depression, Fluoxetine, Immunity.

Introduction

A malignant tumor is one of the common diseases that affect human health at present, and its morbidity increases year by year. As a mental disorder, depression is mainly characterized by significant depressing mood, accompanied by corresponding changes in behavior and thinking. Patients often feel down in the dumps together with the feelings of disappointment, decline in mobility, inferiority, and self-blame. In severe cases, patients may have suicidal thoughts. Investigations and researches reported that the suicidal patients with depression accounted for 15% and had become the second burden disease. It not only bothers the lives of patients, but also increases the burdens on society and family. Many clinical studies proved that adverse physiological factors, including depression and anxiety, were significantly correlated with malignant tumor and the morbidity of depression of patients after suffering from malignant tumor could reach 40-45%. Fluoxetine, a selective serotonin reuptake inhibitor (SSRIs), can relieve the depressive symptoms.
of various types of patients with depression. Through conducting comparison and analysis for the observation of 262 patients during their hospitalization, our study provides evidence for clinical psychological intervention. It also provides that fluoxetine can improve the quality of life and immune function of patients with depression after suffering from a tumor.

Patients and Methods

Patients

The research objects were 262 cases of patients hospitalized in oncology department of our hospital and diagnosed as malignant tumor by pathology and imageology. Their composition was as follows: A: Gender: 170 cases of males and 92 cases of females. B: Age: 140 cases with age < 60 years old and 122 cases with age ≥ 60 years old. C: Tumor location: 48 cases with tumor in digestive system, 72 cases with tumor in respiratory system, 23 cases with tumor in breast, 23 cases with tumor in ovary and 20 cases with tumor in other locations. D: Tumor staging: 20 cases of stage I, 35 cases of stage II, 92 cases of stage III and 120 cases of stage IV. E: With or without chronic cancer pain: 102 cases with no cancer pain and 160 cases accompanied with cancer pain. F: Income satisfaction degree: 52 cases were satisfied with income and 210 cases were dissatisfied with income (Figure 1).

Inclusion Criteria

The inclusion criteria of subjects: Adults patients over 18 years old with clinical manifestations and pathological and cytological diagnostic basis. They must be diagnosed by imageology and tumor marker, and they had nothing to do with tumor types and locations.

Exclusion criteria: (1) Patients with severe body diseases, such as cardiovascular and cerebrovascular disease, organ failure, thyroid disease, and diabetes; (2) Psychopathy; (3) Alcohol, drug and medicine addicts; (4) Patients with brain metastases; (5) Patients with mental retardation; (6) Patients with electrolyte disturbance; (7) Poor treatment compliance.

Therapeutic Schemes

We selected fluoxetine, a selective serotonin reuptake inhibitor, as the anti-depression drug in this study. Three weeks after being diagnosed as depressives, patients were treated with fluoxetine to exclude other disturbing factors, including the psychological stress reaction, preliminarily occurred in patients with tumor who were diagnosed as cancer. Fluoxetine was taken orally for 6 weeks, 20 mg/d. Meanwhile, normal anti-tumor treatment was conducted according to the situations of patients.

Research Methods

Our study was a prospective work. The investigation was accomplished from January 2015 to October 2015.

General Condition Questionnaire

The content included: 1. Social characteristics: gender, age, household income, etc.; 2. Disease data: tumor location, pathological staging and whether there is chronic cancer pain.

Depression Evaluation

According to Hamilton Depression Scale (HAMD) (24 items), the classical depression rating scale formulated by Hamilton. Detection was conducted for the selected 262 cases of patients, including depression emotion, feelings of guilt, suicide, difficulty in falling asleep, totaled 24 items, with 0-4 scores for each item. The total scores of this table could not only reflect the severity of depressive symptoms after suffering from tumor, but also better reflect therapeutic effects.

Life Quality Evaluation

At present, quality of life questionnaire (QLQ—C30) developed and formulated by EORTC, is widely used to evaluate related quality of life of patients with tumor. It is also applicable in China. This questionnaire included 15 content items, with each representing three symptoms, namely fatigue, nausea and vomiting, and pain; five functions, namely physical function, cognitive function, emotional function, role function and social function; six individual items, namely shortness of breath, insomnia, anorexia, constipation, diarrhea and economic hardship, and overall quality of life, totaled 30 questions. The higher the overall quality of life and various functional dimensions were, the higher the quality of life was. The higher the scores of the last two items were, the poorer the functions were.

Detection of Immunity Indexes

About 2 ml venous blood was collected on empty stomach at early morning from control group
and treatment group 6 weeks after being treated with fluoxetine. Lymphocyte subsets applied CD3, CD4, CD8, CD4/CD8, and NK cells. The model of flow cytometry was FACSVantage SE.

Statistical Analysis
The analysis of data applied SPSS17.0 software (SPSS Inc., Chicago, IL, USA). The statistical data were expressed as mean ± standard deviation (SD). The comparison of gender, age, tumor staging, pathogenic site, income satisfaction and chronic cancer pain between the group without depression and the group with depression applied chi-square test. The two independent sample t-test was used for comparison between research group and control group, while the paired t-test was used for comparison of the research group, before and after treatment. p < 0.05 indicated that there was a statistical difference.

Results
Figure 2 shows the basic data of patients of group without depression and group with depression. Table I shows the results of statistical
Prevalence of depression in tumor patients and fluoxetine effects

We could find from the table that the two groups had no statistical difference in the pathogenic site of tumor ($p > 0.05$).

The survey results of HADM were shown in Figure 3. Before and after treatment, the HAMD scores of control group had no statistical difference. Before and after being treated with fluoxetine, the HAMD scores of treatment group had statistical significance ($p < 0.05$), which proved that the depression situation of patients had been improved significantly after taking fluoxetine.

QLQ—C30 questionnaire survey in the field of functional symptom. It was found through QLQ—C30 questionnaire that all functions of patients were improved after being treated with fluoxetine. Especially, the adjustment of emotional function had obvious improvement ($p < 0.01$). Physical function, role function, cognitive function and social function had no significant difference, as shown in Figure 4, which proved that fluoxetine could improve the emotional function of patients. Among the main symptoms, the scores of fatigue and pain declined in treatment group, which had statistical significance ($p < 0.05$), while nausea and vomiting had no evident improvement, as shown in Figure 5, which showed that fluoxetine could relieve patients’ feelings of fatigue and pain. Among single symptoms, shortness of breath, appetite, and insomnia had been relieved, which had statistical differ-

Figure 2. Comparison of the number of tumor patients with and without depression.
ence \((p < 0.05)\). Although the scores of appetite, constipation and economic hardship of patients declined, there was no statistical difference, as shown in Figure 6, which showed that the situations of shortness of breath, appetite, and sleep of patients had been improved after the application of fluoxetine. After the administration of fluoxetine, the overall quality of life of patients had been improved, which had statistical difference \((p < 0.05)\), as shown in Figure 6.

T cell subsets before and after treatment (Figures 7-8) showed that the CD4+/CD8+, CD3+, CD4+, and CD8+ of control group and treatment group were comparable and the differences had no statistical significance \((p > 0.05)\). After being treated with fluoxetine, CD3+, CD4+, and CD4+/...
CD8+ increased and CD8+ decreased. Compared with control group, the differences had statistical significance ($p < 0.05$).

Changes of NK cells before and after treatment

The NK cells were $15.8 \pm 11.23$ before treatment. Six weeks after being treated with fluoxetine, the NK cells were $29.01 \pm 2.15$, with an increase of NK cells. Compared with those before treatment, the differences had a statistical significance ($p < 0.01$).

**Discussion**

The malignant tumor is considered as “incurable disease” in traditional view. Patients with tumor often generate severe psychological stress to affect the disease development. In recent years, with the transformation of medical model from traditional biomedical model and the increase of the morbidity of tumor, the influencing factors of tumor-related psychological illness are increasingly valued. As a pathological reaction of emotion, tumor-related depression makes patients lose their personal mental state. Through investigations and studies, many scholars found that psychological and social factors, including depression, anxiety and fear, had great influences on the immune function of tumor patients and
prognosis of patients\textsuperscript{11-13}. Fisch et al\textsuperscript{19} have proved in their studies that the depression emotion of patients with malignant tumor could increase pain sensitivity, decrease immune function of organism, increase adverse reactions and reduce quality of life of patients. As selective serotonin reuptake inhibitor that can indirectly activate NE energy, fluoxetine has effect in the treatment of depression. By virtue of the advantages, including fast onset, good therapeutic effects, and few side effects, it becomes the first-choice drug in the treatment of depression related to various diseases, including malignant tumor. Therefore, early detection and treatment of depression related to malignant tumor can improve the prognosis of patients and improve quality of life of patients\textsuperscript{5}.

In clinical practice, doctor mainly relies on clinical manifestations of patients to make a definite diagnosis of depression, and Hamilton Depression Scale (HAMD) can only be used as an auxiliary tool for depression diagnosis. In our study, we found that tumor-related depression was connected with gender, through analyzing relevant factors of tumor depression, and the morbidity of females was higher than that of males. Breast cancer and female genital system tumor frequently occur in females. Operation treatment may lead to the partial loss of their femaleness, which brings huge psychological effects for them. Meanwhile, females, with delicate feelings, often worry too much about their disease, thus to easily cause the occurrence of depression. The gender is closely related to the occurrence of depression of patients with malignant tumor. Relative to males, females are more easily to suffer from tumor-related depression. There was also a correlation between ageing and the occurrence of depression. The older the age was, the higher the morbidity of patients. This shows that the damage of malignant tumor to physiology directly affects the emotions of patients who are not satisfied with their incomes. There was no statistical significance between the difference of pathogenic sites and tumor-related depression ($p > 0.05$), which might be related to tumor patients’ cognition degree of disease. In conclusion, the results of analysis show that the malignant tumor-related depression is not significantly associated with tumor types. The rate of occurrence of depression is relatively high in female patients, older patients, advanced tumor patients, patients accompanied with chronic cancer pain and patients who are not satisfied with their incomes.

When quality of life is evaluated, QLQ—C30 scale is adopted by a lot literature reports because it includes items that affect quality of life, including fatigue, insomnia, depression, and pain. The aggravated depression emotion can seriously affect the physical function, role function and emotional function of patients to reduce the quality of life and make it hard for patients to integrate into society. In the QLQ—C3 survey in this study, before and after the treatment with fluoxetine in control group, the scores of patients with tumor-related depression in physical function, emotional function, role function and overall quality of life increased, while the scores of pain, fatigue, insomnia, and anorexia decreased. It showed that fluoxetine had significant therapeutic effects on improving physical ability and physical status of patients. Meanwhile, it could relieve depression emotion, improve the fatigue and insomnia, alleviate pain and increase appetite, playing an important role in improving quality of life of patients.

T lymphocyte is a kind of cell colony composed by CD3+, CD4+, and CD8+. However, the balance of cellular immunity is maintained by the ratio of CD4+/CD8+. If the ratio increases, it means that the immune response of organism plays the positive regulatory role.
Otherwise, it can severely affect the immune function of organism29. As total T lymphocytes, CD3+ can promote the activation of T lymphocytes. As helper and inducer T lymphocytes, CD4+ T lymphocytes can enhance organism immunity through cytokines released after its activation. CD8+ T lymphocytes are suppressor T lymphocytes. Therefore, immunoreactions mediated by T lymphocytes are of great importance in antitumor of body. In this study, before the treatment of fluoxetine, CD3+, CD4+, and CD4+/CD8+ of patients with tumor decreased, and CD8+ increased. After drug treatment, CD3+, CD4+, and CD4+/CD8+ of patients with tumor increased and CD8+ decreased. Compared with control group, the differences had statistical significance (\(p < 0.05\)). Results showed that fluoxetine could enhance the immunity of patients with tumor-related depression through adjusting T lymphocytes, thus to improve the quality of life of patients.

NK cells are cells with antitumor effects. After activation, they can diffuse and infiltrate to the source of infection or tumor tissues to play the role of antitumor. Many studies proved that NK cells play an important role in the immune surveillance of tumor. In the treatment of patients with malignant tumor, the combination of traditional scheme and NK cell treatment can increase the immune function of patients, relieve their pain caused by tumor and improve the quality of life of patients. In our study, after the administration of drug, the NK cells of patients increased, which had statistical difference by comparing with control group (\(p < 0.05\)). Results showed that fluoxetine could increase NK cells so as to play its role of antitumor.

Conclusions

In the clinical treatment of tumors, consideration should be given to psychological problems of patients so as to find the tumor-related depression of patients as soon as possible, which is not only mental illness, but also closely related to physical illness. Moreover, fluoxetine is also given for treatment so as to improve the quality of life of patients and enhance organism immunity of patients with tumor.

Conflict of Interest
The Authors declare that they have no conflict of interests.

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