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Effect of Kanglaite combined with chemotherapy on myelosuppression, immune function and tumor markers levels in patients with breast cancer

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ABSTRACT

Objective: To investigate the effect of Kanglaite combined with chemotherapy on myelosuppression, immune function and tumor markers levels in patients with breast cancer. **Methods:** A total of 90 breast cancer patients in our hospital were randomly divided into control group (45 cases) and observation group (45 cases). The two groups received CAF chemotherapy, and the observation group was additionally given Kanglaite injection (200 mL/d) for 2 weeks continuously. Both groups had chemotherapy for 6 courses. The effect on myelosuppression, immune function and tumor markers levels was detected and compared before and after treatment in two groups. **Results:** After treatment, myelosuppression was found in both groups, and the levels of leukocyte, hemoglobin and platelet decreased significantly compared with before treatment (P<0.05). But the decline of leukocyte, hemoglobin in the observation group was lower than that in the control group (P<0.05); After treatment, the levels of immune function indexes ($CD3^+$, $CD4^+$, $CD4^+/CD8^+$) were increased significantly than those before treatment in the observation group (P<0.05), while the level of immune function ($CD8^+$) were decreased significantly (P<0.05). There was no significant difference on immune function indexes ($CD3^+$, $CD4^+$, $CD8^+$, $CD4^+/CD8^+$) in the control group (P>0.05), and the levels of immune function indexes ($CD3^+$, $CD4^+$, $CD4^+/CD8^+$) of the observation group were significantly higher than those in the control group （P<0.05）. After treatment, the levels of two tumor markers (CEA, CA15-3) decreased significantly than before treatment in both groups (P<0.05), and the decrease amplitude in the observation group was higher than that in the control group (P<0.05). **Conclusions:** Kanglaite combined with chemotherapy has evident therapeutic effect on breast cancer. It can alleviate the myelosuppression caused by chemotherapy, improve immune function, and reduce the concentration of tumor markers in patients with breast cancer.

1. Introduction

Breast cancer is the uncontrolled cell proliferation of breast glandular epithelial cells, which experienced gene mutation caused by a variety of combined carcinogenic factors. The levels of tumor markers increases significantly in patients with breast cancer[1−3] . The therapy for breast cancer is dominated by surgery, combined with chemotherapy as a supplement. But many patients are diagnosed as advanced cancer, missing the chance of operation, and can only be treated by chemotherapy. As Long term chemotherapy can lead to myelosuppression and immune suppression, it brings great physical and mental damage to patients[4,5]. Kanglaite, an antineoplastic preparation, is extracted from the Chinese herbal medicine coix seed. And it has obvious inhibition and killing effect on most of the tumor cells. This research aims to investigate the effect of Kanglaite and chemotherapy on myelosuppression, immune function and tumor markers levels in patients with breast cancer.

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2. Materials and methods

2.1. General data

A total of 90 breast cancer patients admitted July 2013-July 2015 were randomly divided into control group and observation group, each of 45 cases. The observation group: 32-65 years old, average age (45.66±7.92), TNM stage III: 25 cases, TNM stage Ⅳ: 20 cases. The control group: 34-65 years old, average age (46.83±7.85), TNM stage III: 26 cases, TNM stage Ⅳ: 19 cases. Inclusion criteria were as follows: All patients accorded with relevant diagnostic criteria of the breast cancer; Patient card's functional status (Karnofsky) score was not lower than 60; All patients were expected to survive more than half a year. And they should be excluded with allergy to treatment drugs. They did not have a history of chemotherapy and radiotherapy, contraindications of chemotherapy, and had no heart, liver and renal function problems, blood system diseases, or hypertension, diabetes mellitus. This study was reviewed by ethics committee. All patients were volunteered to participate in this study and signed the informed consent. General information showed no significant difference between patients in the two groups and was comparable.

2.2. Method

Patients in the two groups received CAF chemotherapy, namely: Cyclophosphamide 500 mg/m^2, doxorubicin 50 mg/m^2 and fluorouracil 750 mg/m^2, intravenous injected on 1 D; All patients were treated with six cycles of chemotherapy and 21 days was a cycle. On the basis of chemotherapy, patients in the observed group were also given dose of 200 mL Kanglaite injection vein infusion therapy, 1 times a day for 2 weeks continuously.

2.3. Observation of indexes

Fasting peripheral blood of patients was collected in the morning. And Perlong medical XFA6100A blood detector was used to detect blood coagulation indexes of white blood cell, hemoglobin and platelet. Changes of the lymphocyte subsets, CD3$^+$, CD4$^+$, CD8$^+$, CD4$^+$/CD8$^+$ were determined and analyzed with the flow cytometry before and after the treatment. While using double antibody sandwich chemiluminescence detection method for detecting the level of cancer embryo antigen (CEA) and cancer antigen 153 (CA15-3), the kit is from Beijing HuaDaji BiAi Biological Technology Co., Ltd. All operations were strictly enforced in accordance with the instructions.

2.4. Statistics analysis

Using SPSS 18 software, the measurement data was expressed as mean±standard deviation. The difference between groups was compared by t test, and $P < 0.05$ was regarded as statistically significant difference.

3. Results

3.1. Comparison of myelosuppression before and after the treatment

Before treatment, the levels of leukocyte, hemoglobin and platelet of patients in two groups showed no significant difference (P>0.05). After treatment, myelosuppression was found in both groups, and the levels of leukocyte, hemoglobin and platelet decreased significantly compared with before treatment (P<0.05). And the decline of leukocyte, hemoglobin in the observation group was lower than that in the control group (P<0.05) (Table 1).

3.2. Comparison of immune function of two groups before and after treatment

Before treatment, there was no significant difference on immune function indexes (CD3$^+$, CD4$^+$, CD8$^+$, CD4$^+$/CD8$^+$) between the two groups (P>0.05) After treatment, the levels of immune function indexes (CD3$^+$, CD4$^+$, CD4$^+$/CD8$^+$) were increased significantly than those before treatment in the observation group (P<0.05), while the level of immune function (CD8$^+$) were decreased significantly (P<0.05). There was no significant difference on immune function indexes (CD3$^+$, CD4$^+$, CD8$^+$, CD4$^+$/CD8$^+$) in the control group (P>0.05). And the levels of immune function indexes (CD3$^+$, CD4$^+$, CD4$^+$/CD8$^+$) of the observation group were significantly higher than those in the control group（P<0.05 (Table 2).

Table 1

Changes of leukocyte, hemoglobin and platelet in both groups before and after treatment.

Groups	Time	n	Leukocyte ($\times 10^9$/L)	Hemoglobin (g/L)	Platelet ($\times 10^9$/L)
Observation group	Before treatment	50	5.32 ± 0.33	127.85 ± 18.63	180.82 ± 20.21
	After treatment		3.45 ± 0.21^{ab}	115.61 ± 16.86^{ab}	136.36 ± 24.69^{a}
Control group	Before treatment	50	5.11 ± 0.21	127.94 ± 21.74	182.52 ± 21.69
	After treatment		2.96 ± 0.19^{a}	102.47 ± 21.62^{a}	127.87 ± 22.45^{a}

Note: Compared with before treatment, ^aP <0.05; Compared with the control group, ^bP <0.05.

Table 2

Comparison of immune function of two groups before and after treatment.

Groups	Time	n	CD3$^+$(%)	CD4$^+$(%)	CD8$^+$ (%)	CD4$^+$/CD8$^+$
Observation group	Before treatment	45	46.3 ± 11.2	45.6 ± 10.8	25.9 ± 68	1.8 ± 0.6
	after treatment		58.0 ± 12.8^{ab}	49.8 ± 7.5^{ab}	22.9 ± 6.7^{a}	2.2± 0.7^{ab}
Control group	Before treatment	45	48.2 ± 10.1	48.3± 11.1	24.8 ± 6.9	1.9 ± 0.7
	after treatment		47.9 ± 12.8	44.2± 12.3	24.3 ± 7.7	1.9 ± 0.8

Note: Compared with before treatment, ^aP<0.05; Compared with the control group, ^bP <0.05.

3.3. Changes of tumor markers levels in both groups before and after treatment

Before treatment, the levels of two tumor markers (CEA, CA15-3) showed no significant difference between patients in the two groups (P>0.05). After treatment, the levels of two tumor markers (CEA, CA15-3) decreased significantly than before treatment in both groups (P<0.05). And the decrease amplitude in the observation group was greater than that in the control group (P<0.05) (Table 3).

Table 3

Changes of CEA and CA15-3 levels in both groups before and after the treatment.

Groups	Time	n	CEA (μg/L)	CA15-3 (U/mL)
Observation group	Before treatment	45	59.81 ± 4.60	216.67 ± 36.71
	After treatment		16.81 ± 3.82[ab]	103.60 ± 22.62[ab]
Control group	Before treatment	45	58.69 ± 4.39	215.25 ± 33.63
	After treatment		20.69 ± 4.35[a]	169.27 ± 26.89[a]

Note: Compared with before treatment, [a]P<0.05; Compared with the control group, [b]P<0.05.

4. Discussion

Breast cancer, a systemic malignant tumor, is the uncontrolled cell proliferation of breast glandular epithelial cells, which experience gene mutation caused by a variety of combined carcinogenic factors and damage the breast structure. Breast cancer is the most common clinical cancer in female[6,7]. The clinical therapy for breast cancer is dominated by surgery, and combined with chemotherapy as a supplement. But many patients have missed timing of surgical treatment when diagnosed, and can only be treated by chemotherapy. Although chemotherapy can eliminate a large number of cancer cells, but its selective inhibition effect is not very strong. It has certain toxicity effect on some normal immune active cells, epithelial cells in the GI tract, reproductive cells and other normal proliferative epithelial cells when it kills tumor cells. Together with gastrointestinal reaction induced by chemotherapeutic drugs, all these can lead to immune function suppression and myelosuppression[8,9]. That how to enhance the treatment effect, reduce the concentration of tumor markers, reduce the chemotherapy adverse reaction as far as possible, the immune function suppression and myelosuppression, to improve the quality of patients' life, has become important problems which clinical need to face at present. The purpose of Traditional Chinese medicine treating the tumor is to neoadjuvant chemotherapy, reduce the side-effect of chemotherapy, improve the internal environment and reduce myelosuppression, improve immunity, and enhance the effectiveness of cancer treatment[8,9]. Kanglaite Injection was used in combination with chemotherapy in this study.

Kanglaite injection is the effective anticancer component extracted from coix seed. It is a traditional Chinese medicine injections composed of coix seed oil and soybean lecithin and glycerol supplemented. In the perspective of traditional Chinese medicine, Kanglaite injection can invigorate Qi and nourish Yin, corporeity, scatter extravasated blood and eliminate stagnation. It can assist radiation treatments and chemotherapy, enhance tumor therapeutic effect, and can inhibit development of some cancer lesion[10–13]. It also has some analgesic effect. Studies have indicated that Kanglaite inhibits tumor cells, and controls its metastasis by up regulating gene expression of p53 and down regulating gene expression of bcl-2[14,15]. At the same time, Kanglaite has protective effect on patients' immune system. And it can reduce myelosuppression, improve patients' appetite, and improve the Karnofsky score, playing an important role as well in the prevention of tumor recurrence and metastasis.

Blood routine examination can assist the diagnosis of human hematopoietic function and immune system *etc*., which can reflect the human health condition[12]. Chemotherapy induces the decrease of hematopoietic stem cells mitosis, and inhibits the proliferation of bone marrow cells, thus leads to hematopoietic dysfunction[16]. In this study, patients in two groups experienced myelosuppression after treatment. And counts of white blood cell, hemoglobin and platelet were significantly decreased compared with before treatment (P<0.05). The decrease amplitude of white blood cells, hemoglobin in observation group was significantly greater than that of control group (P<0.05). This showed that Kanglaite injection can reduce breast cancer patients with myelosuppression caused by chemotherapy significantly.

The occurrence and development of tumor is closely related to patients′ immune function condition, among which cellular immune function of T lymphocyte is especially important. The detection of T lymphocyte subsets is an important type in monitoring the immune function[17]. On the surface of $CD3^+$ T lymphocyte are CD3 molecules, which is composed of 6 peptide chains and often combines with TCR. $CD4^+$ is an important immune cells type in the human immune system, which is mainly expressed in helper T cells. $CD8^+$, expressed in the cytotoxic T cell, can suppress the synthesis and secretion of antibody, and can inhibit the growth of T cells. The ratio of $CD8^+$ to $CD4^+$/ is an indicator of immune regulation[18]. Therefore, when the $CD4^+/CD8^+$ value is abnormal, immune function disorder occurs. This research results showed that after treatment, the levels of immune function indexes ($CD3^+$, $CD4^+$, $CD4^+/CD8^+$) were increased significantly than those before treatment in the observation group (P<0.05), while the level of immune function ($CD8^+$) were decreased significantly (P<0.05). There was no significant difference on immune function indexes ($CD3^+$, $CD4^+$, $CD4^+/CD8^+$) in the control group (P>0.05), and the levels of immune function indexes ($CD3^+$, $CD4^+$, $CD4^+/CD8^+$) of the observation group were significantly higher than those in the control group (P<0.05). It Suggested that Kanglaite injection can improve the immune function of patients with breast cancer significantly, and can reduce the chemotherapy caused by immune suppression.

CEA[19] was first found in colon cancer and fetal bowel tissues. CEA, a glycoprotein, can cause immune response in patients as antigen. There is a tiny amount of CEA in healthy bodies, but it elevates in many sorts of patients with tumors. And serum CEA will

also increase in 15%-53% of smokers, pregnancy and diabetics. So the specificity of CEA is not high, and its sensitivity is not high either. Its effect on early diagnosis of tumor is not obvious, and is often combined with other tumor markers to detect tumors. The concentration of Serum CEA is under 2.5 g/mL in 97% of healthy adults. Its positive rate is also very high in breast cancer patients, generally in 50%-70%. CA15-3 is the most important specific marker for breast cancer[20]. It often elevates in breast cancer patients, but its sensitivity is low in the early stage of breast cancer, about 60%. While the positive rate can reach 80% in metastatic breast cancer. The dynamic detection of CA15-3 levels in patients is helpful for early detection of tumor recurrence in patients with stage II and stage III breast cancer. Patients with elevated CA15-3 level in breast cancer patients have a earlier incidence of tumor metastasis than in normal patients. When CA15-3 level is higher than 100 U/mL, it can be considered that a metastatic lesion has occurred. Results of this study suggested that After treatment, the levels of two tumor markers (CEA, CA15-3) decreased significantly than before treatment in both groups (P<0.05), and the decrease amplitude in the observation group was higher than that in the control group (P<0.05). It showed that KLT can induce the apoptosis of tumor cells, kill the cancer cells, and can decrease the concentration of tumor markers CEA and CA15-3 significantly in patients.

In summary, Kanglaite injection combined with chemotherapy has remarkable effect on the treatment of breast cancer. It can reduce the myelosuppression induced by chemotherapy, improve the immune function ,and reduce the tumor markers concentration in the patient's body. It is worthy of clinical popularization and application.

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