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Effect of compound radix sophorae flavescentis injection combined with Xiaoyao pill on breast cancer

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ABSTRACT

Objective: To investigate the influence of compound radix sophorae flavescentis injection and Xiaoyao pill combined therapy on tumor markers, cytokines and lymphocyte subpopulations of breast cancer patients, thus provide relevant assistance on clinical therapy for breast cancer patients. **Methods:** A total of 170 breast cancer patients treated in our hospital were selected and divided to be the observe group and control group at random, 85 cases for each group. For patients in control group, AC chemotherapeutic project was utilized, and for patients in observe group, compound radix sophorae flavescentis injection and Xiaoyao pill combined therapy were provided on the basis of AC chemotherapy. Tumor markers, cytokines and lymphocyte subpopulations of breast cancer patients in each group were detected before and after therapy. **Results:** Comparison of tumor markers, cytokines and lymphocyte subpopulations levels between the two groups of breast cancer patients before therapy showed no statistical significant difference (P>0.05). Compared with prior therapy, the tumor markers (CA153, CEA and CYRA21-1), $CD8^+$ and cytokines (IL-4, IL-6 and IL-10) on both the two groups of breast cancer patients were dramatically decreased, while lymphocyte subpopulations ($CD3^+$, $CD4^+$, $CD4^+/CD8^+$), IFN-γ and IL-2 were significantly increased (P<0.05). **Conclusions:** Compound radix sophorae flavescentis injection and Xiaoyao pill combined therapy can significantly improve the tumor markers, cytokines and lymphocyte subpopulations of the breast cancer patients. It is of vital clinical significance for treatment on breast cancer patients.

1. Introduction

As a common female malignant cancer, breast cancer is the most common pathogeny which could cause death of women[1]. Morbidity of female breast cancer presents a rising trend, and the increasing rate has been reached to 3%-4%. In addition, women with breast cancer have been tended to be younger, which brought to heavy burdens for the families[2,3]. Chemotherapy is a normal therapeutic method for cancer, although it has been achieved satisfied therapeutic effects, the side effects could still influence on the cancer therapy, physical and mental health for the patients[4]. How to effectively release or prevent the adverse reactions due to chemotherapy becomes a key of cancer chemotherapy[5]. Our research investigated the mechanism of compound radix sophorae flavescentis injection combined with Xiaoyao pill to treat breast cancer, and provided relevant assistance on clinical therapy for breast cancer patients.

2. Materials and methods

2.1. General data

Our research was conducted after permission received from ethic committee in our hospital and informed consent forms signed by the patients. A total of 170 breast cancer patients treated in our hospital were selected from May 2013 to May 2016. Histopathological tests were done to diagnosed patients with breast cancer. And all

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the patients were met the diagnose standards of NCCN Breast Cancer Clinical Practice Guidelines and the therapeutic standards of chemotherapy. All patients were randomly divided to be two groups, the observe group and the control group. There were 85 cases in observe group, the age range was 35-55 years old, and the average age was (48.8±4.5) years old. The 85 cases included 35 cases of invasive ductal carcinoma, 12 cases of mucinous carcinoma, 28 cases of invasive lobular carcinoma and 10 cases of medullary carcinoma; There were 85 cases in observe group, the age range was 35-55 years old, and the average age was (49.5±4.2) years old. The 85 cases included 36 cases of invasive ductal carcinoma, 11 cases of mucinous carcinoma, 27 cases of invasive lobular carcinoma and 11 cases of medullary carcinoma. For all the patients, Karnofsky scores were $\geqslant$60, the lifetime cycles were predicted to be more than 6 months, and no metastasis phenomenon appeared. There was no difference in ages, genders, tumor positions, types, stages, differentiates, sizes and physical conditions between the two groups of patients (P>0.05). Every breast cancer patient were checked, no other diseases appeared, such as cardiac, intestine, kidney, liver, pulmonary, endocrine. They had never received any treatment in the recent three months, and they could active cooperation with the relevant treatments.

2.2. Therapeutic methods

For patients in control group, AC chemotherapeutic project was provided: 60 mg/m2 Adriamycin (Shanxi Pude pharmaceutical Limited by Share Ltd, Approved number: H14023143), 600 mg/m^2 Cyclophosphamide (Jiangsu Hengrui pharmaceutical Limited by Share Ltd, Approved number: H32020856); For patients in observe group, compound radix sophorae flavescentis injection (Shanxi Zhendong Pharmaceutical Limited by Share Ltd, Approved number: Z14021231) injected via intramuscular route 2-4 mL per time, 2 ×/day, and Xiaoyao pill (Henan Province Wan Xi pharmaceutical Limited by Share Ltd, Approved number: Z41021831), 8 pills one time, 3×/day were provided on the basis of the chemotherapy; For both of two groups, 21 days was a course.

2.3. Indexes detection

A total of 5 mL peripheral blood were extracted before treatment and after treatment for 21 days for breast cancer patients in both control group and observe group, and sent to the clinical laboratory to detect relevant indexes. ELISA method was used to measure arbohydrate antigen (CA153), carcinoembryonic antigen (CEA), cell keratin fragments antigen (CYFRA21-1), interferon-γ (IFN-γ), interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-6 (IL-6) and interleukin-10 (IL-10). The kits were provided by Hangzhou Dian Bang Biological Technology Co., Ltd., Shanghai Jiang Lai Biotechnology Co., Ltd., Shanghai Super Research Biotechnology Co., Ltd., Shanghai Heng Fei Biological Technology Co. Ltd. and Shanghai Tong Wei Industrial Co., Ltd. The enzyme micro-plate reader (Nanjing Germany Iron Laboratory Equipment Co., Ltd., Model number: HBS-1096A) was utilized to measure the OD value at 450 nm. Then the corresponding concentrations were calculated by standard curves. The manipulate process was strictly followed instructions; The flow cytometry (Beckman Kurt, Model number: CytoFLEX, USA) was used to detect $CD3^+$, $CD4^+$, $CD8^+$ cell ratio. The relevant antibodies were provided by Shanghai Heng Fei Biological Technology Co. Ltd., and manipulations were strictly conducted following the instructions.

2.4. Statistical methods

SPSS 18.0 statistical software was utilized to count and analyze the relevant datas. Lymphocyte subgroups, tumor markers and cytokines were expressed by average number±standard deviation. The comparison between the observe group and control group, and for the inter-group were processed by t test. P<0.05 indicated that difference was statistical significant.

3. Results

3.1. Comparison of breast cancer markers between two groups before and after treatment

Before therapy, the differences of tumor markers between the two groups of patients were not statistical significant (P>0.05); After combined therapy, for patients in observe group, tumor markers CA153, CEA and CYRA21-1 were significantly lower than before therapy in this group (P<0.05); For control group after therapy, tumor markers were significantly lower than before therapy (P<0.05); After therapy, for observe group, tumor markers CA153, CEA and CYRA21-1 were significantly lower than control group (P<0.05) (Table 1).

Table 1
Comparison of breast cancer markers between two groups before and after treatment .

Groups	Time	CEA (ng/mL)	CA153 (U/mL)	CYRA21-1 (ng/mL)
Observe group	Prior treatment	11.59±1.42	43.78±4.63	4.95±1.37
	After treatment	5.69±1.02$^{*\#}$	22.67±3.48$^{*\#}$	2.33±0.95$^{*\#}$
Control group	Prior treatment	11.63±1.11	43.82±4.96	4.89±1.20
	After treatment	9.25±1.18*	35.17±4.42*	3.05±1.14*

Note: Compared with prior treatment on the same team, $^{*}P$<0.05; Compared with control group after treatment, $^{*}P$<0.05.

3.2. Comparison of lymphocyte subpopulations between two groups before and after treatment

Before therapy, the difference of lymphocyte subpopulations between the two groups of patients were not statistical significant (P>0.05); After combined therapy, for patients in observe group,

lymphocyte subpopulations $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ were significantly higher than before therapy in this group, $CD8^+$ was significantly lower than before therapy (P<0.05); For control group after therapy, variations of lymphocyte subpopulations were same as which in observe group, the differences were statistical significant (P<0.05); After therapy, for observe group, lymphocyte subpopulations $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ were significantly higher than control group, CD8+ was significantly lower than control group (P<0.05) (Table 2).

3.3. Comparison of cytokines between two groups before and after treatment

Before therapy, the difference of cytokines between the two groups of patients were not statistical significant (P>0.05); After combined therapy, for patients in observe group, cytokines IL-4, IL-6 and IL-10 were significantly lower than before therapy in this group, IFN-γ, IL-2 were significantly higher than before therapy (P<0.05); For control group after therapy, cytokines were significantly lower than which in the same group before therapy (P<0.05); After therapy, for observe group, cytokines IL-4, IL-6 and IL-10 were significantly lower than control group, IFN-γ, IL-2 were significantly higher than control group (P<0.05) (Table 3).

4. Discussion

Breast cancer is a kind of malignancy appeared on the breast epithelial tissue. Most of the breast cancer patients were women. The number has been arrived at 99%[6,7]. So far, breast cancer has been became the most common malignancy happened on women in the world, it was the most common pathogen leading to death of women. The appearance of breast cancer was always closely related with bearing, pollution of environment, hereditary factors and so forth[8]. With the development of society and variation of life habits, morbidity of female breast cancer patients showed an yearly increasing trend. The average increasing speed of breast cancer has been reached to 3%-4%, and tended to be rejuvenation[9,10]. Breast cancer therapy has been became an urgent thing for medical workers. So far, general prognostic effects for breast cancer patients were comparatively ideal. In developing countries, the average cure rate of breast cancer patients already arrived at 57%, but the situation is still rigorous[11,12].

Currently, chemotherapy, surgery and radiotherapy are three normal methods for cancer therapy. These three methods received a considerable development per the long-time application, wide treat range and ideal effects[13]. Meanwhile, many new cancer therapeutic methods appeared, such as immune therapy, photodynamic therapy, photothermal therapy and so on. Still their effects could not equal with chemotherapy[14]. Chemotherapy is a method of cancer treatment using chemical medications to kill tumors. It could overcome the disadvantage of the only local treatments surgery and radiotherapy could be conducted, and could effectively treat the metastasis focus and tumor cells in blood[15]. As a systemic therapeutic method, chemotherapy has favorable therapeutic effects for metastatic tumors[16,17]. However, since chemotherapeutic medications were lack of targeting property, chemotherapy caused the damage of normal cells, and tolerance of tumor cells, so disease recovery of patients were affected[18]. Therefore, while using chemotherapeutic medicines to treat cancer, effectively release the side effects of the medicines could yield twice the result with half the effort[19]. Compound radix sophorae flavescentis injection is a Chinese patent medicine extracted from radix sophorae flavescentis and white Poria cocos. It has vital functions on cooling blood and detoxifying, clearing heat and draining dampness, dissipating and pain killing, *etc*.[20]. Xiaoyao pill could strengthen splenic functions of patients, so that it could regulate the immune functions of patients. In the meantime, it could smooth the liver and resolve masses to decrease the toxicity drug inducted[21]; While treating breast cancer with chemotherapeutic medicines, utilizing of compound radix sophorae flavescentis injection and Xiaoyao pill could better show the therapeutic effects of cancer therapy.

Our research found that effects of compound radix sophorae flavescentis injection combined with Xiaoyao pill could improve

Table 2
Comparison of lymphocyte subpopulations between two groups before and after treatment.

Groups	Time	$CD3^+$ (%)	$CD4^+$ (%)	$CD8^+$ (%)	$CD4^+/CD8^+$
Observe group	Prior treatment	49.24±4.35	33.12±3.56	33.42±3.54	0.95±0.22
	After treatment	57.53±5.08*#	42.35±3.22*#	24.55±2.96*#	1.71±0.27*#
Control group	Prior treatment	49.20±4.28	33.18±2.99	33.36±3.21	0.96±0.20
	After treatment	52.67±4.93*	36.21±3.76*	28.61±3.00*	1.23±0.24*

Note: Compared with prior treatment on the same team, *P<0.05; Compared with control group after treatment, *P<0.05.

Table 3
Comparison of cytokines between two groups before and after treatment.

Groups	Time	IFN-γ (pg/L)	IL-2 (pg/L)	IL-4 (pg/L)	IL-6 (pg/L)	IL-10 (pg/L)
Observe group	Prior treatment	635.26±15.16	8.95±0.47	4.18±0.28	4.65±0.33	4.62±0.29
	After treatment	838.02±17.20*#	12.79±0.56*#	2.35±0.36*#	2.38±0.25*#	2.44±0.15*#
Control group	Prior treatment	632.84±14.33	8.88±0.58	4.22±0.30	4.71±0.40	4.58±0.32
	After treatment	692.58±16.85*	10.73±0.42*	3.28±0.24*	3.69±0.32*	3.38±0.23*

Note: Compared with prior treatment on the same team, *P<0.05; Compared with control group after treatment, *P<0.05.

the tumor markers, cytokines and lymphocyte subpopulations levels of breast cancer patients who received chemotherapy. And the effects are better than simple AC chemotherapeutic project. Compound radix sophorae flavescentis injection is an important preparation extracted from radix sophorae flavescentis and white poria. A large amount of researches indicated that it had effects of anti-cancer, inflammation diminishing and pain easing, immunity improvement. Compound radix sophorae flavescentis injection could block the tumor cells into the G_2 stage, and effectively suppress the proliferation of tumor cells; Meanwhile, it could accelerate the expression of anti-transfer factor 23 nm, then promote the cell apoptosis. It is important that compound radix sophorae flavescentis injection could inhibit the generation of vessels in the tumor location, and diminish the supplementation for nutrients of tumor cells. Killing tumor cells could be beneficial to decreasing of relevant cytokines. Compound radix sophorae flavescentis injection could significantly improve the immune function of patients, strengthen the lethality and activity of NK, and improve the ratio of T lymphocyte subpopulations on patients. Main ingredients in Xiaoyao pill are radix bupleuri, white paeony root, angelica and ginger, *etc*. Xiaoyao pill could play an important role not only in improving the immune function of patients, but also in improving liver and kidney functions. It could effectively diminish the damage of chemotherapeutic medicines to liver and kidney functions, and prevent the appearance of inflammation on liver and kidney, thus the relevant cytokines levels could be enhanced. The improvement of immune function and inflammatory reaction could be beneficial to cancer therapy and recovery of body functions for patients.

In a nutshell, combination of compound radix sophorae flavescentis injection and Xiaoyao pill could significantly improve the tumor markers, cytokines and lymphocyte subpopulations levels for breast cancer patients. It has of vital clinical significance on therapies of breast cancer patients.

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