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# Effect of rabdosia rubescens combined with new assistant chemotherapy on serum CA199, CEA, CA15−3 and T lymphocyte subsets in patients with breast cancer

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ABSTRACT

**Objective:** To study the effects of Rabdosia rubescens combined with neoadjuvant chemotherapy on serum CA199, CEA, CA15-3 levels and T lymphocyte subsets in patients with breast cancer. **Methods:** A total of 70 patients with breast cancer in our hospital were enrolled as the subjects of this study. The subjects were divided into control group ($n$=35) and treatment group ($n$=35) randomly. Patients in the control group were treated with new assistant chemotherapy, while those who were in the treatment group were treated with rabdosia rubescens combined with new assistant chemotherapy. The two groups of patients were treated for 3 periods. The serum CA199, CEA, CA15-3 levels and peripheral blood $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ cells of the two groups before and after treatment were compared. **Results:** There were no significantly differences among the serum CA199, CEA, CA15-3 levels and peripheral blood $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ cells of the two groups before treatment. The serum CA199, CEA and CA15-3 levels of the two groups after treatment were significantly lower than those before treatment, besides, the serum CA199, CEA and CA15-3 levels of the treatment group were significantly lower than those of the control group. The peripheral blood $CD4^+$, $CD4^+/CD8^+$ cells of the control group after treatment were significantly lower than before treatment, and the peripheral blood $CD4^+$, $CD4^+/CD8^+$ cells of the treatment group after treatment were significantly higher than those of the control group. **Conclusion:** Rabdosia rubescens combined with new assistant chemotherapycan can significantly reduce the serum CA199, CEA and CA15-3 levels, and improve peripheral blood $CD4^+$, $CD8^+$, $CD4^+/CD8^+$ levels of patients with breast cancer. It is worthy of clinical application.

## 1. Introduction

Breast cancer is a common malignant tumor in women. With the progress of the disease, there are more than 80% of the patients with breast cancer in vivo transfer of exfoliated cancer cells, lymph, blood free after spread to the brain, lung, liver, bone, skin, pleura and other organs, endangering the life safety of patients[1,2]. In recent years, with the change of women's social role and the pressure of survival, the incidence of breast cancer has been increasing year by year, posing a serious threat to the health of the vast number of female groups[3]. Therefore, thorough, prompt and effective treatment of breast cancer is of great significance in the clinic. At present, the clinical treatment of breast cancer mainly adopts radiotherapy, chemotherapy and surgery, but the effect is not satisfactory[4]. In recent years, with the promotion and in-depth study of Chinese medicine, the combination of Chinese and Western medicine treatment of breast cancer has attracted the attention of researchers, and is an important breakthrough point of treatment. Rabdosia rubescens is a Labiatae Isodon plants, its mian components is oridonin, and it has certain curative effect on gastric cardia cancer, esophageal cancer, pancreatic cancer, primary liver cancer, prostate cancer and other cancers[6,7]. The purpose of this study was to study the effects of Rabdosia rubescens combined with neoadjuvant chemotherapy on serum CA199, CEA, CA15-3 levels and T lymphocyte subsets in patients with breast cancer. The results are as follows.

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## 2. Materials and methods

### 2.1. General information

A total of 70 patients with breast cancer in our hospital from January 2015 to January 2017 were enrolled in this study. Case inclusion criteria: (1) The patients were diagnosed as breast cancer by pathological puncture test; (2) The expected survival time was more than 3 months; (3) No anticancer drugs have been used in the past six months. Case exclusion criteria: (1) Acute infection patients; (2) Patients with other malignancies; (3) Chemotherapy and chemotherapy contraindicated patients; (4) Patients with hepatic or renal dysfunction; (5) Pregnant or lactating women.

The 70 subjects included in this study were randomly divided into control group and experimental group, with 35 cases in each group. Patients in the control group were aged from 32 to 66 years old and their mean ages are (46±8) years old; The pathological stage: 18 cases of stage II, 11 cases of stage III , 6 cases of stage IV ; pathological type: 19 cases of invasive ductal type, 13 cases of invasive lobular, 2 cases of adenoid carcinoma, 1 case of medullary carcinoma; molecular subtypes: 2 cases of Luminal type A, 1 case of Luminal type B ,17 cases of H type , and 15 cases of triple-negative. In the experimental group, patients were aged from 33 to 65 years old, with mean age of (47±9) years old; The pathological stage : 17 cases of stage II, 13 cases of stage III, 5 cases of stage IV ; pathological type: 20 cases of invasive ductal type, 11 cases of invasive lobular, 2 cases of adenoid carcinoma, 2 case of medullary carcinoma; molecular subtypes:1 case of Luminal type A, 1 case of Luminal type B ,19 cases of H type , and 14 cases of triple-negative. The general data of age, pathological stage, pathological type and molecular subtype of the two groups were not statistically significant ($P$>0.05), and the cases were comparable. The two groups of patients were informed of the study before the treatment, and signed the informed consent with consent. The study was approved by the medical ethics committee of our hospital.

### 2.2. Experimental methods

The control group was treated with neoadjuvant chemotherapy with taxanes and anthracyclines treatment, specifically: docetaxel (purchased from Chen Xin Pharmaceutical Limited by Share Ltd, specifications 60 mg/branch, National Drug Certificate H20057404), 175 mg/m$^2$, intravenous drip; epirubicin (purchased from Pfizer Pharmaceutical (Wuxi) Co., Ltd., specifications 50 mg/branch, National Drug Certificate H20000496), 70 mg/m$^2$, intravenous injection; 3 W for 1 cycles, 3 cycles for 1 course. Patients in the experimental group were given Rabdosia rubescens (purchased from Anyang Huaan Pharmaceutical Co., Ltd., standard 0.255 g/piece, National Drug Certificate Z20023064) combined therapy based on the treatment in control group, specifically: Chemotherapy with control group; Donglingcao tablets, oral, 5 tablets each time, 3 times/d. Two groups of patients were given continuous treatment for 3 courses.

### 2.3. Detection index

Collect 10 mL venous blood of an empty stomach in the morning of two groups before and after treatment, and 5 mL venous blood was centrifuged with a centrifuge 10 min to separate serum with a speed of 3 000 rpm, then detect and compare serum levels of CA199 (carbohydrate antigen 199), CEA (carcinoembryonic antigen)and CA15-3 (carbohydrate antigen 15-3) in two groups before and after treatment. The other 5 mL was used to detect and compare the ratio of $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ cells in peripheral blood before and after treatment in the two groups.

The levels of serum CA199, CEA and CA15-3 were detected by double sandwich enzyme-linked immunosorbent assay kit (purchased from Nanjing Jinyibai Biological Technology Co. Ltd.). Backman CytoFLEX flow cytometry was used to detect the ratio of $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ cells in peripheral blood.

### 2.4. Result analysis

We Used SPSS 19.0 software package to process the test result data, mean ± standard deviation (Mean ± SD) represents measurement data, the use of t test was to compare the difference between groups; and $\chi^2$ test was used to count the data in terms of rate (%),with $P$<0.05 as a statistically significant.

## 3. Results

### 3.1. Comparison of serum CA199, CEA and CA15–3 levels before and after treatment in two groups

Before treatment, the levels of serum CA199,CEA and CA15-3 in the control group were (91.25±11.18) U/L, (49.14±8.33) μg/L and (45.47±7.52) U/mL respectibvely， and those in the experimental group were (90.68±10.51) U/L, (49.61±9.15) μg/L and (46.07±8.05)

Table 1.
Comparison of serum CA199, CEA and CA15-3 levels before and after treatment in two groups.

| Group | $n$ | Time | CA199 (U/L) | CEA (μg/L) | CA15-3 (U/mL) |
|---|---|---|---|---|---|
| Control group | 35 | Before treatment | 91.25±11.18 | 49.14±8.33 | 45.47±7.52 |
| | | After treatment | 47.53±6.20$^*$ | 26.84±5.49$^*$ | 19.33±4.11$^*$ |
| Experimental group | 35 | Before treatment | 90.68±10.51 | 49.61±9.15 | 46.07±8.05 |
| | | After treatment | 19.31±5.14$^{*\#}$ | 11.20±3.05$^{*\#}$ | 9.14±3.24$^{*\#}$ |

Note: compared with before treatment, $^*P$<0.05; compared with the control group, $^\#P$<0.05.

Table 2.
Comparison of T lymphocyte subsets in peripheral blood between two groups before and after treatment (%).

| Group | *n* | Timr | $CD4^+$ | $CD8^+$ | $CD4^+/CD8^+$ |
|---|---|---|---|---|---|
| Control group | 35 | Before treatment | 33.65±2.40 | 24.58±2.17 | 1.37±0.47 |
| | | After treatment | 28.21±2.05* | 24.05±2.26 | 1.17±0.38* |
| Experimental group | 35 | Before treatment | 34.08±2.87 | 25.11±2.59 | 1.36±0.42 |
| | | After treatment | 32.55±1.95# | 24.23±2.40 | 1.34±0.39# |

Note: compared with before treatment, *$P$<0.05; compared with the control group, #$P$<0.05.

U/mL. There was no significant difference between the two groups ($P$>0.05); After treatment, the levels of serum CA199, CEA and CA15-3 in the control group were (47.53±6.20) U/L, (26.84±5.49) μg/L and (19.33±4.11) U/mL and those in the experimental group were (19.31±5.14) U/L, (11.20±3.05) μg/L and (9.14±3.24) U/mL. The serum levels of CA199, CEA and CA15-3 in the two groups were significantly lower than before treatment, and the serum levels of CA199, CEA and CA15-3 in the experimental group were significantly lower than those in the control group, and the difference was statistically significant ($P$<0.05), shown in the Table 1.

### *3.2. Comparison of T lymphocyte subsets in peripheral blood between two groups before and after treatment*

Before treatment, the ratios of $CD4^+$,$CD8^+$ and $CD4^+/CD8^+$ cells in the peripheral blood of the control group were (33.65±2.40)%, (24.58±2.17)% and (1.37±0.47)%, those in the experimental group were (34.08±2.87)%, (25.11±2.59)% and (1.36±0.42)%; there was no significant difference between the two groups ($P$>0.05); After treatment, the ratios of $CD4^+$,$CD8^+$ and $CD4^+/CD8^+$ cells in the peripheral blood of the control group were (28.21±2.05)%, (24.05±2.26)% and (1.17±0.38)%, those in the experimental group were (32.55±1.95)%, (24.23±2.40)% and (1.34±0.39)%. The ratios of $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ cells in the peripheral blood of the control group were significantly lower than those before treatment, while the ratios of $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ cells in the peripheral blood of the experimental group were significantly higher than those of the control group; the difference was statistically significant ($P$<0.05), shown in Table 2.

## 4. Discussion

At present, thought the pathogenesis of breast cancer is not clear, some research believe that it is related with geographical factors, family history, endogenous or exogenous estrogen stimulation, breast atypical hyperplasia, long-term excessive intake of high fat, high material level ionizing radiation and carcinogenicity of RNA virus infection[8]. Since breast cancer spread to the skin, fascia, chest muscle and other parts, coupled with the patient's body resistance decreased significantly, it is difficult to conduct clinic treatment, mainly using comprehensive treatment measures[9,10]. At present, the main treatment of breast cancer is to prolong the life of patients, improve the quality of life and alleviate the clinical symptoms[11]. Neoadjuvant chemotherapy is a direct and lethal treatment that can reduce tumor immune suppression in patients by directly killing tumor cells[12,13]. Chinese medicine believes that breast cancer belongs to a "breast rock" or "stone milk carbuncle" category, mainly triggered by emotional disorders, eating disorders and Chongren imbalance or pathogen invasion, which leads to induce liver disharmony and imbalance of Yin and Yang, therefore, it should be treated with Fuzheng Guben Xiaoliu[14,15]. Rabdosia rubescens, also known as broken mia, prolific in Hebei, Henan, Gansu, Shanxi, Hunan, Hubei, Anhui, Guangxi and other places, effective components of oridonin, it has certain curative effect on malignant tumor of colon cancer, liver cancer, esophageal cancer, and it has no obvious influence on liver, kidney and bone marrow function[16,17]. This study was to explore the effects of Rabdosia rubescens combined with neoadjuvant chemotherapy on serum CA199, CEA, CA15-3 levels and T lymphocyte subsets in patients with breast cancer so as to provide some guidance for the clinical treatment of breast cancer.

The results showed that after treatment, serum CA199, CEA and CA15-3 levels were significantly lower in the two groups than those before treatment, while the serum levels of the patients in the experimental group were significantly lower than those in the control group (all $P$<0.05). This suggests that Rabdosia rubescens combined with neoadjuvant chemotherapy can significantly reduce the levels of serum CA199, CEA and CA15-3 in patients with breast cancer. CA199 is a kind of lipid that exists in the cell membrane in the form of mucin, in which the level of serum increases gradually with the development of breast cancer[18]. CEA is a non-specific tumor marker, and can be used for the diagnosis and prognosis evaluation of digestive tract malignancies, pancreatic cancer, breast cancer, lung cancer and other diseases[19]. CA15-3 is a breast cancer specific antigen, produced by multiple glands and secreted by multiple epithelial mucin, and is used for the evaluation of recurrence and metastasis of breast cancer[20]. It has been reported that Oridonin can prevent cell mitosis, cause accumulation of cells in phase G2+M, and its inhibitory effect on tumor cell proliferation is obvious. The combination of Rabdosia rubescens and neoadjuvant chemotherapy can kill and inhibit breast cancer cells, thus significantly reducing the levels of serum CA199, CEA and CA15-3 in breast cancer patients. In addition, the results showed that the ratio of $CD4^+$, $CD8^+$ and $CD4^+/CD8^+$ cells in peripheral blood of patients in the control

group was significantly lower than that before treatment, the ratio of $CD4^+$,$CD8^+$ and $CD4^+/CD8^+$ cells in the peripheral blood of the experimental group was significantly higher than that of the control group, and the differences were statistically significant ($P<0.05$). This suggests that Rabdosia rubescens combined with neoadjuvant chemotherapy can significantly improve the level of immune T lymphocyte subsets and enhance immunity. This may be due to the protective effect of Rabdosia rubescens on T lymphocyte subsets by inhibiting vascular endothelial growth factor, which is beneficial to protect the immune function of the patients[22,23].

In conclusion, Rabdosiae neoadjuvant chemotherapy combined with breast cancer patients can significantly reduce serum CA199, CEA and CA15-3 levels, improve the level of immune T lymphocyte subsets and enhance immunity. It is worthy of clinical application

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