Research Article

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Evaluation of the clinical efficacy of preoperative neoadjuvant chemotherapy combined with endocrine therapy for breast cancer

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Objective: To analyze the clinical efficacy of preoperative neoadjuvant chemotherapy combined with endocrine therapy for breast cancer.

Methods: 50 cases of breast cancer patients without surgery treated in our hospital from December 2016 to June 2017 were randomly selected and divided into two groups, of which 25 patients in the control group were treated with neoadjuvant chemotherapy, and 25 patients in the observation group were treated with neoadjuvant chemotherapy plus endocrine therapy. The curative effect, CA153 and CA125 levels, quality of life and incidence of adverse reactions were compared between the two groups.

Results: After treatment, the total response rate in the observation group was 64.0% (16/25), which was significantly higher than that in the control group (32.0% (8/25)). The difference was statistically significant ($P<0.05$). The levels of CA153 and CA125 after treatment in the observation group were significantly lower than those of the control group (12.17 ± 1.8 *vs.* 21.12 ± 2.4, 13.96 ± 2.2 *vs*. 23.32 ± 2.6, respectively), the difference was statistically significant ($P<0.05$). The total effective rate of improvement in the quality of life of the observation group was significantly higher than that of the control group (88.0% (22/25) *vs*. 56.0% (14/25)), the difference was statistically significant ($P<0.05$). The incidence of clinical adverse reactions was lower in the observation group than in the control group, but the difference was not statistically significant ($P>0.05$).

Conclusion: The implementation of preoperative neoadjuvant chemotherapy combined with endocrine therapy in patients with breast cancer can significantly reduce the primary tumor of the patient without increasing the incidence of adverse reactions in patients. It can improve the quality of life of the patients and improve the rate of breast conserving surgery or resection of the patients.

Keywords: preoperative ▪ neoadjuvant chemotherapy ▪ endocrine therapy ▪ breast cancer

Introduction

Breast cancer has been the most frequently occurred malignant tumor in female, which belongs to a systemic disease. We can be informed that the mortality rate of breast cancer ranks the second place in all kinds of cancer in the world according to the relevant data. In recent years, the incidence of breast cancer in postmenopausal women has been gradually increased. Multidisciplinary treatments have been applied in clinic in order to gain more effects by optimizing the clinical efficacy. Neoadjuvant chemotherapy is often used in some breast cancer patients who are inoperable. Compared with adjuvant chemotherapy after conventional surgery, neoadjuvant chemotherapy can make it easier to observe the changes in the therapeutic effects of chemotherapy drugs on tumors, thus helping us gain more knowledge of the efficacy of those drugs. Meanwhile, preoperative chemotherapy can reduce the tumor to a certain extent, reduce the tumor stage of the patient, and thus providing opportunities for the surgical treatments. At the same time, preoperative chemotherapy is able to gain a certain advantage for the feasibility of breast-conserving surgery [1,2]. The chemotherapy response to the neoadjuvant chemotherapy observed in

clinic could be a benchmark for the evaluation of the outcomes. For those patients with locally advanced breast cancer and patients with large tumors (>2CM), neoadjuvant chemotherapy could be a new treatment, which can improve the therapeutic effects. In recent years, the proportion of patients with breast cancer who are clinically positive in estrogen receptor (ER) and/or progesterone receptor (PR) has gradually increased. Therefore, endocrine therapy is usually used before surgery, the effects of which are similar to the chemotherapy [3]. To further analyze the clinical effects of preoperative neoadjuvant chemotherapy combined with endocrine therapy for patients with breast cancer, 50 cases of breast cancer patients without receiving surgery who were treated in our hospital from December 2016 to June 2017 were selected, they received the neoadjuvant chemotherapy or neoadjuvant chemotherapy combined with endocrine therapy in this study. The clinical efficacy of the patients in both groups were compared. The detailed information was shown as below.

Material and methods

General information

50 cases of breast cancer patients without surgery treated in our hospital from December 2016 to June 2017 were randomly selected and divided into two groups. In the control group, 25 patients were (56.8 ± 4.1) years old, and the tumor diameter was (4.2 ± 0.4) cm. The clinical stages of the patients were 14 patients in stage II and 11 in stage III. The pathological diagnosis was infiltrative lobular carcinoma in 4 cases and invasive ductal carcinoma in 21 cases. In the observation group, 25 patients were (55.9 ± 4.4) years old, and the tumor diameter was (4.3 ± 0.6) cm. The clinical stages of the patients were 13 patients in stage II and 12 in stage III. The pathological diagnosis was infiltrative lobular carcinoma in 3 cases and invasive ductal carcinoma in 22 cases. The comparison between the basic data of the control group and the observation group was comparable (P>0.05).

Inclusion criteria

Imaging and histopathologic diagnosis were used to diagnose breast cancer; those who were menopause ER and / or PR positive; patients were aged between 53 and 70 years, stage II-III for breast cancer; informed consent were signed for this study.

Exclusion criteria

Non-menopausal patients; patients had chemotherapy contraindications or allergic constitution; patients with severe liver and kidney dysfunction or other malignancy; patients who have lost the opportunity to receive surgical treatment.

Methods

Neoadjuvant chemotherapy was performed in all patients, and intravenous infusion with 500 mg/m^2 cyclophosphamide, 100 mg/m^2 epirubicin, and 500 mg/m^2 5-fluorouracil mixture was performed. 28 days of continuous chemotherapy was set as a cycle, and the clinical effect was observed after the patients were treated for 2 cycles. The patients in the observation group were treated with endocrine therapy on this basis of receiving the above treatment, using oral treatment with letrozole, 2.5 mg/ time and once a day. Also, 28 days of continuous treatment was set as a cycle, and the clinical efficacy was observed after 2 cycles.

Determination of the tumor markers

The venous blood samples were taken from all patients before and one week after the treatment. Serum was extracted by centrifugation and preserved in -20°C for determination.

Specimen examination: the specimen was configured according to the ratio of 1/21 with sample diluent. The contrast fluids and the test specimens of tumor markers (CA153 and CA125) were shaken at 37°C for 40 min using a micro-constant temperature oscillator (Changzhou Langyue Instrument Manufacturing Co., Ltd.). After the plates were washed in a fully automatic plate machine (Jinan Gaokui Medical Devices Co., Ltd.), the enzyme antibody solution was added. The plate was shaken and washed again, and then the luminescent liquid was added and the plate was examined under a biochip reader (manufactured by Changzhou Langyue Instrument Manufacturing Co., Ltd.).

Observation indexes

The evaluation standard for the short-term effects of the patients with solid tumors: It was defined as complete remission (CR) when the patient's tumor was completely

disappeared and the condition could be remained for more than four weeks. Partial relief (PR) was determined when the product of the maximum diameter of the tumor was reduced by more than 50%. When there was no change in the maximum diameter of the tumor, we concluded it to be no change (NC). The overall response rate was the sum of CR rate and PR rate.

The adverse reactions in the two groups of patients were analyzed, including nausea and vomiting, thrombocytopenia and bone marrow suppression, and the incidence of adverse reactions in the two groups was compared.

The Karnofsky score was used to assess the quality of life of the patients. We concluded it to be improved when the Karnofsky score after treatment was 10 points more than the score obtained before treatment. When the score gained a ≤ 10 points increase, we defined it as stable, and the declined effect was judged when a decrease of more than 10 points was detected after treatment. The total effective rate was the sum of the improvement rate and the stability rate.

Statistical analysis

The data obtained in this study were statistically analyzed using SPSS 21.0. The patient's age, tumor diameter and other measurement data were expressed as standard deviations and t-test was performed for the analysis these measurement data. The enumeration data such as the treatment effects and the incidence of adverse reactions were expressed as the percentage, and X^2 test was performed for such data. P<0.05 indicated a statistically significant difference between the two groups of data.

Results

Comparison of the total response rate between the two groups

After treatment, the total response rate in the observation group was 64.0% (16/25), which was significantly higher than that in the control group (32.0% (8/25)). The difference was statistically significant (P<0.05) (**TABLE 1**).

Comparison of the CA153 and CA125 levels before and after treatment in two groups of patients

The levels of CA153 and CA125 in the observation group after treatment were significantly lower than those of the control group (12.17 ± 1.8, 13.96 ± 2.2 *vs.* 21.12 ± 2.4, 23.32 ± 2.6), the difference of which was statistically significant (P<0.05) (**TABLE 2**).

Comparison of the total effective rate of the improvement of quality of life in the two groups

The total effective rate of improvement in the quality of life of the observation group was significantly higher than that of the control group (88.0% (22/25) *vs.* 56.0% (14/25)), the difference of which was statistically significant (P<0.05) (**TABLE 3**).

The incidence of adverse reactions in the two groups

The incidence of clinical adverse reactions was lower in the observation group than in the control group, but the difference was not statistically significant (P>0.05) (**TABLE 4**).

Table 1. Comparison of the total response rate between the two groups [case (%)]

Group	Case	CR	PR	MR	NC	Total effective rate
Observation group	25	7(32.0)	9(32.0)	8(32.0	1(4.0)	16(64)
Control group	25	2(8.0)	6(24.0)	13(52.0)	4(16.0)	8(32)
X^2	-	-	-	-	-	4.925
P	-	-	-	-	-	<0.05

Table 2. Comparison of the CA153 and CA125 levels pre- and post-treatment in two groups of patients($\bar{x} \pm s$, U/ml)

Group	Case	CA153		CA125		T	P
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment		
Observation group	25	60.98 ± 3.2	*12.17 ± 1.8	76.41 ± 4.6	*13.96 ± 2.2	16.541	<0.05
Control group	25	59.23 ± 4.1	*21.12 ± 2.4	75.16 ± 4.8	*23.32 ± 2.6	19.152	<0.05
T		2.131	4.246	1.094	6.153	-	-
P		>0.05	<0.05	>0.05	<0.05	-	-

Note: "*" was the comparison of the values obtained pre- and post- treatment in each group.

Table 3. Comparison of the total effective rate of the improvement of quality of life [case (%)]

Group	Case	Improved	Stable	Declined	Total effective rate
Observation group	25	12(48.0)	10(40.0)	3(12.0)	22(88.0)
Control group	25	6(24.0)	8(32.0)	11(44.0)	14(56.0)
X^2	-	-	-	-	4.8611
P	-	-	-	-	<0.05

Table 4. The incidence of adverse reactions in the two groups [case (%)]

Group	Case	Nausea and vomiting	Thrombocytopenia	Bone marrow suppression	The incidence of adverse reactions
Observation group	25	14(56.0)	9(36.0)	11(44.0)	34
Control group	25	15(60.0)	11(44.0)	13(52.0	39
X^2	-	-	-	-	14.231
P	-	-	-	-	>0.05

Discussion

Neoadjuvant chemotherapy is a kind of systemic treatment to be applied in a patient before a localized treatment is determined. The use of neoadjuvant chemotherapy in patients with breast cancer can theoretically eliminate the micrometastases in patients, effectively prevent the growth of metastases after primary treatment, and also prevent the emergence of drug-resistant clones [4,5]. The main clinical values of neoadjuvant chemotherapy include: it is able to effectively achieve the early treatment of micrometastases; it can help to rationally evaluate the chemotherapeutic responses of primary tumors; it can effectively reduce the size of primary tumors, and provide conditions for patients undergoing breast-conserving surgery. In the clinical study conducted by Hung et al. [6], they have proposed that neoadjuvant chemotherapy can help improve the disease-free survival rate and overall survival rate of patients with locally advanced breast cancer. Preoperative endocrine therapy is an important method in the preoperative treatment for the patients with positive postmenopausal hormone receptor. It is more applicable to some patients who are not suitable for chemotherapy. In patients undergoing neoadjuvant chemotherapy combined with endocrine therapy, the tumor diameter can be significantly reduced, after which the surgical treatment could then be considered [7,8]. Now there are few studies on the preoperative neoadjuvant chemotherapy combined with endocrine therapy, whose main role is to significantly reduce the estrogen levels in patients, and to inhibit the growth and reproduction of tumor cells. It is more suitable for the postmenopausal patients with ER and (or) PR receptor positive. In fact, the use of letrozole in patients with endocrine therapy could show good safety and reliability, and it can provide good conditions for the patient undergoing surgical treatment. The adverse reactions and chemotherapy reactions after the application of letrozole are relatively weak, making it more acceptable for those patients. Kidachadkar et al. [9] have pointed out that the total effective rate of letrozole was significantly higher than that of tamoxifen in the treatment of postmenopausal breast cancer patients in the clinical study, but the difference in overall survival indicators was not significant. In our study, we found that the CA153 and CA125 levels in the observation group were 12.17 ± 1.8 and 13.96 ± 2.2 U/mL respectively after treatment, which were significantly better than those in the control group (CA153 and CA125 levels being 21.12 ± 2.4 and 23.32 ± 2.6 U/mL). Besides, the overall effective rate of solid tumor in the observation group was 64.0%, which tended to be higher than that in the control group (32%). The total effective rate of the improvement of quality of life was 88.0%, which was significantly higher than that in the control group (56%), showing significant difference in the above two indexes between the two groups. Breast cancer patients with ER and (or) PR receptor-positive were selected and enrolled in the treatment of neoadjuvant chemotherapy combined with letrozole. Results have shown that this combination therapy can significantly reduce the tumor size of the patient and improve the chances for the patient to receive surgery. In this study, the incidence of adverse reactions

in the observation group was lower than that in the control group. To some extent, neoadjuvant chemotherapy combined with endocrine therapy would not increase the incidence of adverse reactions and it was more acceptable for the patients.

At present, preoperative neoadjuvant chemotherapy combined with endocrine therapy is difficult, the main reason is that neoadjuvant chemotherapy could be applied in the patients who are diagnosed with local advanced patients. In order to make the determination to use the combination treatment, doctors should examine the hormone receptors in the tumor tissues, for the fact that only those patients with positive hormone receptors can accept this combination treatment, but the positive rate of hormone receptors in women is about 50% in our country [10]. In the process of population aging, medical insurance gradually covers more elderly patients, despite of this, both doctors and patients may have a better understanding on the clinical values of endocrine therapy, which will furtherly promote the application of endocrine therapy in the preoperative treatment for the patients with breast cancer [11]. In this study, 50 patients with breast cancer were selected as the subject, and the effect of neoadjuvant chemotherapy combined with endocrine therapy in the preoperative treatment of breast cancer was analyzed. Additionally, we also analyzed the effects of neoadjuvant chemotherapy combined with endocrine therapy on the solid tumors, quality of life as well as the adverse reactions. However, we failed to investigate its impacts on the survival rate and recurrence rate, we know that a larger number of samples is needed for this study to furtherly explore the values of this combination treatment and thus providing new path for the treatment of patients with breast cancer [12,13].

In summary, the preoperative implementation of neoadjuvant chemotherapy combined with endocrine therapy in patients with breast cancer can significantly reduce the primary tumor lesions without increasing the incidence of adverse reactions in patients, and help to improve the quality of life, thereby enhancing the probability of the patients to undergo breast-conserving surgery or resection surgery [14,15]. As one of the systemic diseases, the treatment of breast cancer requires the active application of comprehensive treatment. Neoadjuvant chemotherapy is one of the important methods for the clinical treatment of breast cancer. In clinical practice, individual treatment needs to be adopted according to the differences in patients in order to improve the treatment efficacy of neoadjuvant chemotherapy. The choice of clinical treatment plan needs to be furtherly investigated, so as to significantly improve its clinical effects and improve the quality of life of the patients.

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