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Role of Xihuang capsule combined with albumin-bound paclitaxel on the treatment of stage III breast cancer and T cell subsets, survival rate and adverse reactions

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Abstract: To investigate the impact of Xihuang Capsule combined with albumin-bound paclitaxel on the treatment of stage III breast cancer and T cell subsets, survival rate and adverse reactions. Totally 200 patients with stage III breast cancer were evenly randomized into control group (albumin-bound paclitaxel for chemotherapy) and observation group (Xihuang Capsules for adjuvant therapy based on the treatment of the control group). The RR and DCR of the observation group was markedly higher as compared to the control group (66.7% vs 28.6%; 80.9% VS 47.6%) (all P <0.05). After 4 weeks of treatment, the $CD8^+$ in the two groups decreased, while CD3+ and CD4+ increased, and the change in observation group was more significant (all P<0.05). The observation group exhibited a better half-year, 1-year, 1.5-year and 2-year survival rates compared to the control group (81.0% vs 71.4%, 71.4% vs 57.1%, 57.1% vs 33.3% and 42.9%vs 19.0%) (all P<0.05). Adding Xihuang Capsule to adjuvant therapy with albumin paclitaxel chemotherapy benefits the patient's immunity and survival rate, with good efficacy and safety profiles.

Keywords: Breast cancer, chemotherapy, Xihuang capsule, adverse reactions, immune function.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer in female in China. As a systemic disease, the primary means of breast cancer treatment remains surgical intervention, for instance radiotherapy and chemotherapy (Mao *et al*., 2019). Neoadjuvant chemotherapy can eliminate micro metastasis of breast cancer, reduce residual disease, and improve the survival rate and quality of life of patients. Yet, chemotherapy alone always results in massive adverse reaction, which is not conducive to the recovery of patients. Therefore, an essential element in current clinic medicine is to conduct a research targeted at the seeking for drugs that reduce the toxicity of breast cancer chemotherapy (Yang *et al*., 2020). Xihuang Capsule has a role in detoxification, dissipating masses, reducing swelling and relieving pain, which is applicable in disease syndromes caused by poison-blood stasis. Its combination with albumin-bound paclitaxel are proved to be encouraging in the clinical efficacy and safety (Zhu *et al*., 2016; He *et al*., 2018). The main goal of the current study is to investigate the effect of Xihuang Capsule combined with albumin-bound paclitaxel in the treatment of stage III breast cancer and its influence on T cell subsets, survival rate and adverse reactions.

MATERIALS AND METHODS

210 cases of stage III breast cancer patients admitted to our hospital starting January 2018 to January 2020 were randomized into the control group and the treatment group. The control group was 53-68 (60.00±4.24) years; pathological types: 30 cases of invasive lobular carcinoma, 75 cases of invasive ductal carcinoma; Karnofsky Performance Status (KPS) score was (80.81±2.34) points; there were 65 cases of lymphatic metastasis and 40 cases without lymphatic metastasis. The observation group was 51-67 (59.57±4.21) years old; pathological type: 25 cases of invasive lobular carcinoma, 80 cases of invasive ductal carcinoma; KPS score was (80.67±2.31) points; there were 75 cases of lymphatic metastasis, and 30 cases with no lymphatic metastasis. They were of comparability with respect to the general data (P>0.05). This study was approved by the Medical Ethics Committee of our hospital and obtained the consent from the patients and their families.

Inclusion criteria

(1) Meeting the diagnostic criteria for breast cancer and its TNM staging; (2) Female aging 45 to 60 years; (3) First breast cancer chemotherapy; (4) KPS score > 60 points, expected survival time > 3 months; (5) No chemotherapy contraindications; (6) No Chinese medicine treatment within 4 weeks before enrollment.

Exclusion criteria

(1) With a history of cancer; (2) Mental disorders; (3) Bilateral breast cancer; (4) Severe liver and kidney dysfunction, endocrine disorders and other diseases; (5) Allergic to the drugs in this study.

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Treatment methods

Patients in the control group were given albumin-bound paclitaxel (Qilu pharmaceutical (Hainan) Co., Ltd; batch number H20193309, specification 100mg/bottle) intravenously for 30 min, once every 3 weeks, 260mg/m^2 each time. 21 d is a course of treatment for 3 consecutive courses; the observation group was given Xihuang Capsule (Shijiazhuang Dongfang Pharmaceutical Co., Ltd.; batch number Z20053216, specification 0.25 g×24 capsules) 6 capsules once on the basis of the control group, 2 times/d and the course is the same as the control group.

Outcome measures

T lymphocyte subsets CD3+, CD4+, CD8+. Peripheral blood nucleated cells were separated by density gradient centrifugation with lymphocyte separation medium, nucleated cells in peripheral blood were stained and labeled for 30 min, hemolyzed for 10 min, centrifuged at 300 g for 5 min, discarded the supernatant, washed twice with PBS, and then flow cytometry was used to detect serum T lymphocyte subsets CD3+, CD4+, CD8+.

Karnofsky Performance Scale (KPS). KPS reflects a person's ability to perform certain ordinary tasks. We used KPS to measure the quality of life of cancer patients. KPS ranking runs from 100 to 0, where 100 is perfect health and 0 is death (Wu *et al*., 2018).

Efficacy evaluation. According to the RECIST evaluation criteria (He *et al*., 2018), the patient's condition is classified into progressive disease (PD), stable disease (SD), partial remission (PR) and complete remission (CR) to evaluate the treatment effect of solid tumors. Disease control rate (DCR) = (SD + PR + CR) /total number of cases × 100%, and total effective rate (RR) = (CR + PR) / total number of cases × 100%.

Survival rate. All patients were followed up for two years, and their half-year, 1-year, 1.5-year and 2-year survival rates were recorded and compared.

STATISTICAL ANALYSIS

All data analysis was performed with SPSS23.0 software. The measurement data were expressed in the form of (mean ± standard error) and verified via t test; while the enumeration data were represented by cases and percentage, and processed by χ 2 test. A *P* value of <0.05 indicated that the difference was statistically significant.

RESULTS

Short-term efficacy

The chi-square test shows that both DCR and RR of the observation group was markedly higher as compared to the control group (66.7% vs 28.6%; 80.9% VS 47.6%) (both *P* <0.05) (table 1).

Quality of life scores before and after treatment

Regarding the KPS scores, the control group and observation group before treatment were (67.62±0.50) points and (67.57±0.93) points, respectively and the scores after treatment were (80.67±2.31) points and (80.81±2.34) points, respectively. And the t-test reveals no statistical difference in KPS scores before and after treatment (t = 0.208, 0.199, *P*>0.05, table 2).

T cell subsets

The results of t-test detected no significant difference in CD3 +, CD4 +, CD8 + between the two groups prior to treatment (*P*>0.05). After 4 weeks of treatment, the CD8 $^+$ in the two groups decreased and the reduction in observation group was more notable (*P*<0.05). While CD3+ and CD4+ were increased and the increase in observation group was much higher (*P*<0.05) (table 3).

Survival rates

With respect to half-year, 1-year, 1.5-year and 2-year survival rates, the chi-square test demonstrates remarkably better outcomes in observation group vs. Control group in 1.5-year and 2-year survival rates (57.1% vs 33.3% and 42.9%vs 19.0%) (*P* <0.05) (table 4).

DISCUSSION

Around 1.3 million people worldwide are diagnosed with breast cancer every year, and approximately 400,000 of them die from the disease (Su *et al*., 2018). Some patients have recurrence and metastasis after surgery, or distant metastasis had occurred at the time of diagnosis, and basically lost the chance for radical treatment. For such patients, the general intent of treatment is not only to reduce the focus, but also to raise the patient's quality of life (Li *et al*., 2018). Chemotherapy is currently one of the more mature and effective means to promote tumor cell apoptosis and inhibit cancer cell metastasis, of note, its adverse reactions are also commonly recognized and documented (Fu *et al*., 2020). In recent years, comprehensive treatment of traditional Chinese medicine has been acknowledged the clinical community of oncology at home and abroad because of the excellent progress it made in this research field (Wang *et al*., 2020).

Breast cancer is classified as milk rock and other diseases in the literature related to traditional Chinese medicine. Due to the long-term repeated stimulation of various internal and external factors, the meridians are blocked, the Qi and blood, and the viscera are imbalanced, causing the accumulation of turbid evil. It accumulates to develop into tumors over time (Zhao *et al*., 2020).

Table 1: Comparison of short-term efficacy of patients [n(%)]

Groups	PD	SD	PR	CR	DCR	RR
Observation group	20	15	45	25	17(80.9)	14(66.7)
Control group	55	20	25	5	10(47.6)	6(28.6)
X^2						7.328
P						0.009

Table 2: Comparison of quality of life scores before and after treatment

Groups	N	KPS score	
		Before treatment	After treatment
Observation group	105	67.57±0.93	80.81±2.34
Control group	105	67.62±0.50	80.67±2.31

Table 3: Comparison of two groups of T cell subgroups

Groups	CD3 +		CD4 +		CD8 +	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Observation group	33.90±5.36	50.13±4.88	34.06±4.97	44.13±4.58	30.73±4.01	21.11±4.39
Control group	35.34±3.33	43.60±4.54	31.34±4.44	35.28±4.67	31.34±3.33	26.40±4.49
t	1.047	4.494	1.871	6.189	0.535	3.853
P	0.301	0	0.069	0.001	0.595	0

Table 4: Comparison of adverse reactions and survival rates [n%]

Groups	survival rate			
	half a year	one year	one year and a half	two years
Observation group	85(81.0)	75(71.4)	60(57.1)	45(42.9)
control group	75(71.4)	60 (57.1)	35 (33.3)	20(19.0)
X^2	8.096	6.786	7.899	7.085
P	0.034	0.543	0.032	0.024

On the basis of the patient's visceral dysfunction, cancer toxin further has an impact on the transfusion and metabolism of Qi, blood and body fluid, leading to blood stasis in the veins and dampness to condense into phlegm. Cancer toxins endogenously block the Qi, the Qi cannot flow through the blood, and the blood clotting further forms blood stasis. Cancer toxins, phlegm and blood stasis promote the development of breast cancer (Wu *et al*., 2020).

Paclitaxel is extracted from *Taxus brevifolia*, which has a role in inhibiting the depolymerization of microtubules, causing abnormal arrangement of microtubules, and killing cancer cells. It has been widely used in cancer treatment (Xu *et al*., 2020). The albumin-bound paclitaxel manufactured by nanotechnology can be rapidly distributed to tissues, allowing the drug to accumulate in tumor tissues. Albumin-bound paclitaxel is distributed quickly, and the drug concentration is higher than that of conventional polyoxyethylene-ricin toxin paclitaxel preparations (Yang *et al*., 2021). Importantly, the intravenous infusion time can be shortened to 30 min without anti-allergic pretreatment. Xihuang Capsules are mainly composed of artificial bezoar, artificial musk, myrrh, and frankincense. The artificial bezoar in the prescription is fragrant and cold in nature, which has a significant impact on clearing heat and detoxification, reducing phlegm, eliminating swelling, and relieving pain. Musk is fragrant and has a pungent nature and capable of passing through the twelve meridians, which is known for its function as promoting blood circulation, dispersing stagnation, clearing meridians, dispelling viciousness, and removing filth (Lee *et al*., 2020; Costa *et al*., 2018; Costa *et al*., 2017). Bezoar-made musk strengthens the function of bezoar to reduce phlegm and eliminate swelling. The combination of frankincense and myrrh can exert influence in promoting blood circulation and Qi, stimulating menstruation, reducing swelling and relieving pain. Taken together, the integration of above 4 drugs can soften and relieve lumps, clear heat and detoxification, eliminate phlegm, dispel stasis, and relieve pain (Guo *et al*., 2018; Li *et al*., 2020; Guo *et al*., 2015; Wang *et al*., 2020; Sun *et al*., 2020).

In this study, the DCR and RR of the observation group was markedly higher as compared to the control group.

Whereas no statistical difference was observed in KPS scores both before and after treatment. Additionally, after 4 weeks of treatment, the $CD8^+$ in the two groups decreased, and the reduction in observation group was more notable as compared to the control group. While $CD3^+$ and $CD4^+$ were increased, and the increase in observation group was much higher. All these suggested that the adjuvant treatment of Xihuang Capsules with albumin-bound paclitaxel chemotherapy obtain excellent results in patients with advanced breast cancer and enhance the immune function of patients. Moreover, the observation group exhibited a better outcome as compared to the control group considering the half-year, one-year, 1.5-year and 2-year survival rates. It is shown that the addition of Xihuang Capsule to the observation group for adjuvant treatment can effectively reduce the occurrence of adverse reactions, improve the quality of life of the patients, and prolong their survival time. However, the major issue in the present study that how both drugs interact and the specific formula or equation used for the calculation remains unknown. Therefore further studies to explore what and how the exact function of each drug are required.

CONCLUSION

To conclude, adding Xihuang Capsule to adjuvant therapy with albumin-bound paclitaxel chemotherapy can obtain excellent outcomes with respect to patient's immunity and survival rate, with remarkable clinical efficacy and low adverse reactions.

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