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Original Article

Effect of Self-Controlled Exercise on Antioxidant Activity of Red Blood Cells and Functional Recovery of Limbs in Patients with Breast Cancer after Rehabilitation

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Abstract

Background: We aimed to investigate the effect of self-controlled exercise on the antioxidant activity of red blood cells and the recovery of limb function in patients with breast cancer after rehabilitation.

Methods: Overall 130 breast cancer patients admitted to the First Affiliated Hospital of Zhengzhou University, China from Feb 2018 to Jan 2019 were divided into intervention group and control group. The control group received perioperative care and chemotherapy, the intervention group implemented a self-controlled exercise program. Indexes were compared between the two groups before intervention, 3 months and 6 months after intervention.

Results: The activity of erythrocyte superoxide dismutase (SOD) in the intervention group was significantly increased in the first 3 months (P=0.030), and decreased from 3rd to 6th month (P=0.033). The glutathione peroxidase (GSH-Px) activity in the intervention group increased through the whole intervention period. The plasma malondialdehyde (MDA) in the intervention group was significantly decreased (P=0.029, 0.012). After intervention for 3 months and 6 months, the 6MND distances in the intervention group were significantly longer (P=0.001, 0.045). The average exercise time in the intervention group were significantly increased (P=0.004, 0.000).

Conclusion: Self-controlled exercise can effectively improve the antioxidant ability of red blood cells in patients with breast cancer, improve the mobility of shoulder joints of the affected side and increase their exercise capacity, with good sustainability. It has positive effect on postoperative rehabilitation, could be used in long-term regular clinical work.

Keywords: Self-controlled exercise; Breast cancer; Rehabilitation; Antioxidant; Red blood cells

Introduction

Breast cancer is a malignant tumor of breast epithelial tissue and is one of the common female malignant diseases (1). Surgery and chemotherapy are important methods for the treatment of breast cancer (2). The activity of red blood cell superoxide dismutase (SOD), glutathione peroxidase (GSH-Px) plays an important role in maintaining the body's redox reaction balance (3).

Breast cancer has slower development, higher differentiation, weaker invasive ability and better biological characteristics than other tumors (3). However, during chemotherapy, 5-HT3 is released from the cell due to cell death, causing vagal reflex, bone marrow inhibition, etc., and with the increase of the number of chemotherapy, the plasma and erythrocyte lipid peroxide levels are increased and the antioxidant capacity is inhibited to varying degrees. Therefore, the body's rehabilitation was affected (4). Half a year after surgery is a critical period for the recovery of limb function in breast cancer patients (5). Appropriate exercise can effectively maintain the body's redox and prevent the risk of joint adhesion and scar tissue formation.

Self-controlled exercise advocates movement, dynamic and static, in order to achieve the goal of improving the hypoxic state of cancer patients with maximal oxygen uptake. At present, self-controlled exercise is increasingly used for patients with malignant tumors (6).

Therefore, this study explored the effect of self-controlled exercise on erythrocyte antioxidant activity and limb function recovery in breast cancer patients, in order to improve exercise tolerance during chemotherapy and provide new ways to promote continuous exercise.

Materials and Methods

Research object

Overall, 130 patients with breast cancer admitted to the First Affiliated Hospital of Zhengzhou University (Zhengzhou, China) from Feb 2018 to Jan 2019 were enrolled. Inclusion criteria: complete surgical treatment, first chemotherapy after surgery, and hospitalization time ≥ 7 days; pathological examination confirmed breast cancer; mentally conscious, normal cognitive and sensory function; estimated survival time > 6 months, completed 3 times of chemotherapy, female.

This study was approved by the Ethics Committee of the First Affiliated Hospital of Zhengzhou University. Informed consent was taken from the participants before the study.

Exclusion criteria: those had surgery after chemotherapy; had other serious physical diseases and tumors; had recurrent breast cancer and male breast cancer; had a history of mental illness or psychological disease. According to the hospitalization date, 130 patients were divided into intervention group (2018.2-7) and control group (2018.8-2019.1), 65 cases in each group. Intervention group: 22-62 yr old, average 42.22±7.17 yr old; education level: 15 cases of junior high school and below, 26 cases of high school or secondary school, 24 cases of junior college and above; chemotherapy regimen: 41 cases of cisplatin / carboplatin + taxol, 18 cases of cisplatin + cyclophosphamide + doxorubicin, 8 cases of cisplatin + etoposide + bleomycin; tumor stage: 21 cases of stage I, 36 cases of stage II, 10 cases of stage III. Control group: 24-63 yr old, average 43.62±6.57 yr old; 14 cases of junior high school and below, 29 cases of high school or secondary school, 24 cases of junior college and above; 39 cases of cisplatin+ carboplatin+ taxol, 17 cases of cisplatin + cyclophosphamide + doxorubicin, 11 cases of cisplatin + etoposide + bleomycin; 23 cases of stage I, 33 cases of stage II, 11 cases of stage III. There were no significant differences in gender, age, education level, and chemotherapy regimen between the two groups.

Method

Both groups of patients were given routine perioperative care and chemotherapy care. The intervention group began to learn 1 week of self-controlled exercise under the guidance of the researcher at the beginning of the first chemotherapy period, that is, the first day of chemotherapy, and then proceeded 23 weeks of self-controlled exercise, each exercise time 40- 60min, exercise frequency 4 times a week (single day). Self-controlled exercise was a set of sports, consisting of three parts: preparatory activities, whole body exercises, and finishing activities (Table 1).

Table 1: Self-controlled exercise activity time and activity plan

Activity	*Activity time*	*Methods*	*Notes*
Preparatory activity	10 min	Standing warm-up exercise: in order from the neck-shoulder-arms-hands-hip-legs-feet sequence, stretch each part for 10 seconds and then relax for 10 seconds. After all the parts are finished, repeat the practice from the beginning, and then repeat until 10 minutes to achieve the effect of whole body activity.	Background music and guidance, the patient moves each body part following the sequence of the guide and the rhythm
Whole body exercise	35 min		Non-slippery ground, suitable temperature, wear loose and comfortable clothes
		(1) Respiratory self-control: use the nose to inhale and close the lips, inhale twice and exhale once, and breathe in coordination with the upper limb movement and footwork; (2) Upper limb movements: ① Shoulder lifting: put boths hands on the abdomen, lift the shoulders as close as possible to the ear for 10 seconds, and put them down slowly; ② Straight-arm extension, spread both hands to shoulder width, and expand outward to the maximum and kept for 10 seconds, then repeat; ③ Arm folding and lifting: hands overlap on the chest, lift up to 10 seconds and put down, then repeat; ④ backhand stretch: one hand back from the shoulder, the other hand back from the back, hold hands as much as possible, stay for 10 seconds to the maximum.	The background music is a 4-beat rhythm, and the patient follows the lead and rhythm.
		(3) Natural walking: walking at a constant speed in a straight line, walking in a suitable gait, the stride is controlled at 0.45 times of height, and the pace is 1.5 m/s.	Telemetry heart rate monitor is required during exercise
Finishing exercise	5 min	Stand upright, hands naturally hang down, put on the side of the body, swing forward and backward with the pace, adjust the breath until the heart rate drops to 100 beats / min and then ends.	

Quality Control

Safety control: the group exercise was carried out in the ward during the first week. All the researchers were present. All the actions were corrected by the researcher one by one to make sure they were completely mastered before discharge. The family members must be present during the post-discharge activities. During the exercise, the telemetry heart rate monitor should be worn to monitor the heart rate. The maximum exercise intensity setting: maximum heart rate (HRmax)=220-age. When heart rate reached 60% of the maximum heart rate, it was set as medium-intensity exercise, the patient was guided to slow down and reduce the activity intensity to ensure the safety of the event.

Demonstration teaching: the researcher demonstrated and decomposed each action. On Monday, Wednesday and Friday morning, the observation group patients were collectively exercised. One or two patients with better performance were selected to lead the patients to exercise together with the researchers.

Compliance control: at 3 days of admission, 1 day before discharge, 2 sessions of self-control exercise related forum were held. Flower and fruit tea and refreshments favored by women were prepared to encourage patient participation. The Daily Activity Record Form was distributed, families were asked to fill in the patient's daily activity time, activity process, and post-activity response, and data were collected once a week. The WeChat feedback was sent to the researchers on

the weekend. If the feedback was not timely, the researchers will follow up on the phone.

Red blood cell antioxidant activity

Erythrocyte superoxide dismutase (E-SOD), glutathione peroxidase (GSH-Px), plasma malondialdehyde (MDA) activity was important indicators reflecting antioxidant capacity. E-SOD, GSH-Px and MDA were measured by fasting venous blood before intervention, 3 months of intervention, and 6 months of intervention in the early morning.

Joint mobility (7)

After the operation, 3 months, 6 months of intervention, the should joint mobility of the patients was measured by the protractor. The changes of the shoulder joint mobility of the two groups of patients were observed. The range of motion: flexion 0°-180°, extension 0°-60°, 0°-75° for adduction, 0°-180° for abduction.

Measurement of exercise tolerance

Before the intervention, at 3 months of intervention, at 6 months of intervention, 6 min walking test was used to determine exercise tolerance (8). The patients were wearing a telemetry heart rate monitor. They walked straight along the flat ground for 6 min at the fastest speed to measure the walking distance.

Exercise time

Patients were required to record each exercise time (sum of total weekly exercise time/times of exercises per week), weekly exercise time (total exercise time per week).

Results

The antioxidant activities of red blood cells before and after intervention in the two groups

After 3 months of self-controlled exercise, the activity of red blood cell SOD in the intervention group was significantly increased (P=0.030), after intervention for 6 months, SOD was significantly lower than that after intervention for 3 months (P=0.033). Plasma MDA levels in the intervention group at 3 months and 6 months were significantly lower than those before the intervention, and were significantly different from the control group (P=0.029, 0.012). There were significant differences in erythrocyte SOD activity and plasma MDA in terms of time, group and interaction between the two groups (P=0.000), as shown in Table 2.

Table 2: Comparison of antioxidant activities of erythrocytes before and after intervention in both groups

Indicator	*Group*	*Before intervention*	*3 months*	*6 months*	F_{time}	F_{group}	$F_{interaction}$
E-SOD（U/gHb）	Intervention	13595.48±2513.06	17927.34±2006.24	14588.62±2513.85	3.813*	5.262*	4.795*
	Control	13367.55±2629.40	16842.95±1959.38	15275.62±1857.50			
	t	0.829	3.182	3.016			
	P	0.532	0.030	0.033			
GSH-Px （U/gHb）	Intervention	415.33±98.63	428.21±101.30	432.72±104.17	0.926	0.299	0.649
	Control	419.41±93.75	425.36±92.66	429.17±98.19			
	t	0.570	0.388	0.259			
	P	0.495	0.628	0.783			
MDA（nmol/ml）	Intervention	6.23±2.08	3.36±0.83	3.14±0.76	3.695*	4.723*	3.944*
	Control	6.46±1.92	5.64±1.69	4.42±0.88			
	t	0.295	3.745	4.807			
	P	0.776	0.029	0.012			

The comparison of joint mobility between the two groups

The patient's shoulder joint was observed in the intervention group at 3 months and 6 months after operation, the flexion, extension, adduction and abduction activities were significantly greater than those after the surgery and those of the control group (*P*=0.000). The shoulder joint mobility of the two groups was significantly different in terms of time, group and interaction (*P*=0.000) (Table 3).

Comparison of the exercise tolerance of the two groups before and after intervention

The exercise tolerance of the two groups was not significantly different (*P*=0.394).

The 6MND distance of the intervention group at 3 months and 6 months of intervention was significantly longer than that before the intervention, and both were longer than the control group (*P*=0.001, 0.045), there was a significant difference in exercise tolerance between the two groups in time, group and interaction (*P*=0.000) (Table 4).

The average exercise time of the two groups of patients

The differences in weekly average exercise time were statistically significant between groups (*P*=0.004, 0.000) (Table 5).

Table 3: Comparison of joint mobility between the two groups

Indicator	*Group*	*Before intervention*	*3 months*	*6 months*	F_{time}	F_{group}	$F_{interaction}$
Flexion	Intervention	106.40±1.86	128.65±1.24	155.70±2.34	7.118*	5.395*	4.709*
	Control	109.27±1.48	115.77±1.69	129.58±2.68			
	t	0.633	5.385	10.007			
	P	0.568	0.000	0.000			
Extension	Intervention	35.41±1.48	43.18±1.36	49.83±1.24	6.846*	5.335*	5.738*
	Control	36.25±1.73	38.47±1.55	42.35±1.19			
	t	0.429	4.723	6.411			
	P	0.593	0.000	0.000			
Adduction	Intervention	56.50±2.08	65.28±1.59	70.31±1.48	4.637*	7.340*	6.307*
	Control	55.29±1.87	58.72±1.78	61.95±1.80			
	t	0.318	6.056	8.230			
	P	0.796	0.000	0.000			
Abduction	Intervention	129.49±2.46	145.26±1.27	164.37±1.55	7.017*	6.128*	5.409*
	Control	127.37±2.25	138.39±1.75	155.87±1.99			
	t	0.763	6.750	9.479			
	P	0.358	0.000	0.000			

Table 4: Comparison of exercise tolerance before and after intervention in two groups of patients (m)

Group	*Before intervention*	*3 months*	*6 months*	F_{time}	F_{group}	$F_{interaction}$
Intervention	420.53±75.29	558.41±61.36	592.25±47.29	8.490*	6.717*	5.755*
Control	416.85±81.37	515.62±72.84	521.42±50.33			
t	0.729	5.386	2.942			
P	0.394	0.001	0.045			

Table 5: Comparison of average exercise time between the two groups of patients (min)

Group	*Number of exercises*	*Weekly average time*	*Average time*
Intervention	6040	214.55±10.62	52.42±6.37
Control	3357	110.25±13.18	21.30±7.64
t		4.872	8.598
P		0.004	0.000

Discussion

Effects of self-controlled exercise on the antioxidant capacity of red blood cells in patients with breast cancer after chemotherapy

The red blood cell SOD, GSH-Px and total antioxidant activity of tumor patients were much lower than the normal population (9). Molecular biology studies suggested that regular exercise upregulates SOD gene expression, thereby enhancing SOD activity in red blood cells, while reducing NAD (P) H oxidase-mediated production of reactive oxygen species and reducing oxidative stress in the body (10, 11). In the self-controlled exercise, patients exercise from breathing to upper limbs to whole-body activities. The movement of molecules in tissue cells and blood cells is accelerated by the heat-generating effect of exercise, and the increase of the body's biological thermal energy promotes tissue metabolism and effectively improves tissue activity.

Regular physical exercise for 3 months can increase the activity of SOD in endogenous red blood cells and improve the body's antioxidant capacity (12). This conclusion is consistent with the results of this study. The activity of erythrocyte SOD decreased in patients with self-controlled exercise for 6 months in intervention group, whether this is related to the change of patient's body state or the lack of samples in this study, or the lack of follow-up observation time needs further verification.

The results in Table 2 suggested that adhering to self-controlled exercise can improve the oxidative stress state of breast cancer patients and reduce the body damage caused by free radicals. In patients with oxidative stress, plasma MDA levels were significantly higher than in the normal population (13,14). MDA is used as an indicator of the degree of free radical damage in the body. Free radicals in the body can crosslink with unsaturated fatty acids on biofilms, destroying cell biofilms, causing loss of normal physiological functions and deepening malignant transformation of tumor cells. The higher metabolic rate of breast cancer patients led to increased free radical production in the body, resulting in a large amount of MDA (15). Long-term self-controlled exercise in this study kept the plasma MDA level in breast cancer patients at a low level, which may be related to the enhanced antioxidant activity of red blood cell SOD, which reduced the formation and accumulation of MDA lipid peroxide, and effectively reduced the release of MDA into the blood. In addition, this study did not find significant changes in the GSH-Px activity of breast cancer patients in the intervention group after 6 months of self-controlled exercise. Related study has confirmed that moderate-intensity exercise has no significant effect on plasma GSH-Px (16), muscle (16) GSH-Px activity in tumor patients, and this conclusion is consistent with this study. The literature indicated that under certain physiological conditions, tumor cell growth rate is negatively correlated with GSH-Px activity (17, 18). The results of this study showed that the activity of erythrocyte SOD increased and the GSH-Px activity did not change significantly in breast cancer patients during the intervention, suggesting that long-term regular self-controlled exercise has positive significance for tumor suppression.

Effect of self-controlled exercise on the activity of limbs in patients with breast cancer after chemotherapy

The self-controlled exercise in this study was a set of exercise programs to promote the recovery

of limb function according to the physiological characteristics of the patient's breast tissue, the surgical method, the degree of injury of the affected limb and the rehabilitation requirements of the chemotherapy period (19, 20). In this study, patients in the intervention group were characterized by upper limb activity. Upper limb activity can significantly enhance the contraction and stretching ability of the upper limb muscle tissue, reduce the risk of joint adhesion and even scar tissue formation, relieve the upper limb function retiring caused by surgical injury and protect the tissues surrounding the breast by strengthening the shoulder to the arms and then lifting it with both hands (21). The natural footwork not only strengthens the synergistic effect of the patient's back, abdomen and leg muscles on the upper limb muscles, but also enhances the cardiopulmonary function by supplementing the breathing exercise, thereby strengthening the muscle tone of the chest muscles and further improving the patient's mobility (22). It suggested that long-term regular self-control exercise has obvious advantages in improving the mobility of the affected limb during postoperative chemotherapy in breast cancer patients.

Effects of self-controlled exercise on exercise endurance and exercise time in patients with breast cancer

Van pointed out that the postoperative exercise of breast cancer patients should consider the length of exercise duration to ensure effectiveness. If it is too long, it will cause fatigue; if it is too short, it will be difficult to be effective (23). The results in Table 4 showed that the self-controlled exercise effectively prolongs the duration of each exercise and the total duration of exercise, suggesting that the self-controlled exercise can improve the patient's exercise continuity under more exercise times and help the patient achieve a certain exercise intensity. Self-controlled exercise is simple, rhythmic and easy to practice, making the patient's exercise experience more enjoyable, avoiding more ineffective time spent on passive exercise, reducing the physical burden and mental stress of long-term exercise, and is important for improving patient persistence (24,25); and self-controlled exercise is a whole body exercise, which can effectively accelerate the blood circulation of the organs, improve the blood flow perfusion of the tissue, and strengthen the oxygen supply of the damaged tissue, thereby promoting the body's activity endurance (26). Under the condition of ensuring exercise time, breathing and exercise are the basis for maintaining health at a certain time, and good exercise tolerance can effectively avoid fatigue caused by chemotherapy (27). With the control of the disease, the long-term self-controlled exercise enhances the muscle oxygen delivery capacity, accelerates the metabolism of lactic acid products in the body, and further enhances exercise tolerance (28). The results in Table 5 suggested that self-controlled exercise can effectively prolong the period of postoperative chemotherapy activity of breast cancer patients, ensure the intensity of exercise and improve their exercise endurance.

Conclusion

Self-controlled exercise can effectively improve the antioxidant capacity of red blood cells in breast cancer patients, improve the mobility of the shoulder joints of the affected limbs, and increase exercise tolerance, which has good sustainability. It could be widely used in clinic.

Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interest.

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