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Sports on the Curative Effect of Breast Cancer Drug-Loaded Nanoparticle Drug Delivery System

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Abstract: Breast cancer has become one of the malignant tumors with the highest incidence in the world. Malignant tumor is a disease that seriously threatens human health. Surgical treatment is difficult to achieve the ideal effect on advanced malignant tumors with extensive metastasis and recurrence. Based on the above background, the purpose of this article is to study the effect of sports on the curative effect of the drug-loaded nanoparticle drug delivery system against breast cancer. This study explores the effect of different exercise time combined with active peptide-modified drug-loaded nano-drug delivery system on breast cancer targeting; it aims to find ways to promote the effect of drug targeted therapy, and provide the role of exercise in tumor targeted therapy new basis. In this study, a comprehensive therapy of drugs combined with exercise was applied to nude mice bearing breast cancer Bcap-37 to observe the effect of exercise on drug treatment. The results of the study found that the exercise combined with PLA-PLL-RGD nano drug delivery system group was statistically significant compared with the exercise group and the saline group ($p<0.05$). Exercise with different exercise time can significantly promote the targeting effect of PLA-PLL-RGD nano drug delivery system on breast cancer tissue neovascularization. It shows that doing appropriate exercise while targeting tumor therapy can help increase targeted drugs to reach the tumor site, and can effectively inhibit tumor growth. Popularizing it in breast cancer treatment will help improve the recovery rate of patients.

1. Introduction

Breast cancer is one of the most serious malignant tumors worldwide threatening woman's health. Incidence rate and mortality rate of breast cancer rank first in all kinds of cancers. According to statistics, one in nine women will develop breast cancer in their lifetime, and the first stage mortality rate of breast cancer is as much as 15%. In recent years, the incidence rate of breast cancer has been increasing year by year. The incidence rate of breast cancer has ranked the first in the

female tumor in the United States. Incidence rate of incidence rate of breast cancer is increasing by nearly 3% in recent 30 years, and the incidence rate of breast cancer is increasing. The incidence of breast cancer is the first place in the city of women, and its mortality has also increased significantly. The role of exercise in the prevention and treatment of chronic diseases such as hypertension and diabetes has been confirmed by a large number of studies. In 2006, the world health organization described cancer as a controllable disease, and the concept that tumor is a chronic disease has been gradually accepted by people. However, as cancer is a special chronic disease, the research on the role of exercise in the treatment of breast cancer is relatively less. In short, most studies believe that exercise can not only reduce the risk of breast cancer caused by unhealthy lifestyle, but also reduce the risk of breast cancer caused by environmental factors, which plays a preventive role in the occurrence of breast cancer, and this preventive effect has nothing to do with the height of body mass index and family history.

The integration of lipoprotein related or apolipoprotein targeted nanoparticles as drug carriers opens up new therapeutic and diagnostic approaches for nanomedicine. This paper reviews the possibility of constructing drug loaded, recombinant or artificial lipoprotein particles. Robert B made a rigorous evaluation of the advantages and limitations of the lipoprotein vector, and discussed the possible challenges in the future, especially the targeting specificity, the concept of lipoprotein rerouting, and the design of novel lipoprotein mimetic particles targeting apolipoprotein sequence [1]. Juweid reviewed the research progress of RXFP1 targeted drugs in recent years. Juweid discussed the discovery of small molecule agonist P1 and mimetic peptide. Detailed signaling studies summarized the cell-specific signals of peptide mimics and the biased signals of small molecule agonists [2]. Lee I explored the feasibility of simultaneously targeting different secondary DNA structures in diffuse large B-cell lymphoma (DLBCL) to regulate two key oncogenes: myc and BCL2. Combined with the previously identified elliptic peptide and pregnenol derivative, which recognize the DNA structure of Myc G-quadruplex and Bcl-2 i-motif promoter, the combination therapy can reduce the mRNA level of DLBCL cell lines, and then increase the sensitivity to the standard chemotherapy drug cyclophosphamide [3].

The fields of nanotechnology mainly include biology, physics, chemistry and materials science, and the development of new nano materials for biomedical and pharmaceutical applications [4]. Biosynthesis of nanomaterials has effectively controlled various endemic diseases with less side effects [5]. Gold nanoparticles can cross the blood-brain barrier and interact with DNA to produce genotoxic effects. Because of their ability to generate heat, they can target and kill tumors, often used in photodynamic therapy. This photodynamic therapy, one of the most commonly used treatment options, usually removes cancer cells with the help of photothermal energy biosynthesized by nanomaterials. Murakami t reviewed the main applications of gold nanoparticles in biomedical field, such as tumor therapy, amyloid fibrillation inhibitor, transplacental therapy, development of specific stent and drug delivery system [6]. Hao y will demonstrate the latest progress of multi-functional nanoparticle targeted drug delivery (active and passive targeting) in melanoma, nano diagnosis and combination therapy of melanoma, and clinical trials of nanodrug-related melanoma. In addition, they will discuss the current status, challenges and prospects of targeting nanoparticle drugs for melanoma [7]. Compared with other colloidal carriers, gelatin nanoparticles have better stability in biological fluids and can provide the required drug molecular control and sustained release. T kiyuna focused on the effects of different formulations of gelatin nanoparticles on zeta potential, polydispersity index, entrapment efficiency and drug release performance. The main applications of gelatin nanoparticles in drug and vaccine delivery, target tissue gene delivery and nutrient delivery were introduced in order to improve the low

bioavailability of bioactive phytonutrients [8].

The innovation of this paper is as follows

(1) Nanodrugs are introduced into the tumor site and internalized into the tumor tissue and space through cell phagocytosis, so as to reduce the toxic and side effects on healthy tissues.

(2) In addition, the research on the targeting of pla-pll-rgd nano drug delivery system combined with exercise proves that exercise can promote the targeted therapy of pla-pll-rgd nano drug delivery system

2. Nanoparticle Drug Delivery System and Sports

2.1. Antineoplastic Nanoparticles

In recent years, a new type of nano drug delivery system has been developed in the research of nano drugs, which is based on the solid natural or synthetic polymer materials as the carrier, encapsulating the anticancer drugs in the polymer materials, and making the solid particle drug delivery system with the particle size of 50 ~ 1000nm [9-10].

Polymer materials have become the focus of pharmaceutical research [11]. Compared with simple injection of anti-tumor drugs, the injection of nano anticancer agents encapsulated with polymer materials has significant advantages

First, polymer materials have the advantages of targeting. After certain structural modification, polymer materials can increase the targeting of lesion sites through temperature targeting, pH targeting, magnetic targeting and other ways, so that the materials can concentrate on the tumor site, play a guiding role, improve the drug concentration in the tumor site, and increase the drug utilization and curative effect [12]. At the same time, it can reduce the aggression of drugs to reticuloendothelial system (RES), reduce the drug load of other normal tissues, and reduce the damage of drugs to normal tissues, so as to reduce the side effects of drugs and better play the curative effect of drugs.

Second, nano drug carriers are obtained by appropriate preparation and purification methods, with appropriate particle size, particle shape and high drug loading. After all kinds of anti-cancer drugs are wrapped by polymer targeted materials, they have a longer circulation time in vivo, which makes the anticancer drugs release slowly in the tumor site, prolong the drug stay time in the tumor site, and better play the efficacy, Inhibition of tumor growth and disease progression [13-14].

Third, after some structural modification, polymer carrier materials can be biodegradable, and often have good biocompatibility and biodegradability, and low toxicity or non-toxic. The encapsulation of polymer materials can maintain the activity of drug components, improve the efficacy of drugs, and reduce the side effects of drugs on normal human body.

2.2. Targeting Carrier Materials

The current tumor treatment methods have toxic side effects on the entire human body and lack specificity. Not only can the tumor not be treated effectively, but it will also cause great harm to the human body. It is the pain caused by the treatment while the patient is tortured by the disease. In this environment, targeted research on tumor therapy should arise from time to time [15]. Targeted drug delivery refers to the selective delivery of drugs to specific physiological sites, organs, tissues or cells, and the therapeutic effects of drugs on that target site. Selective administration can enhance the activity of the drug at the target site and reduce its side effects in non-target sites, and improve the therapeutic index of the drug [16].

In addition, from the perspective of the biological characteristics of tumor cell growth and metastasis, currently commonly used therapeutic methods such as radiotherapy and chemotherapy cannot effectively inhibit tumor growth and metastasis [17-18]. Only by using targeted drug therapy, delivering the drugs that kill tumor cells directly to tumor cells, and effectively inhibiting the growth of tumor new blood vessels through RGD, can malignant tumors, an invisible killer threatening human health, be fundamentally solved. It can be seen that targeted drug delivery is the most effective way to treat malignant tumors.

The most worthy of exploration and the most critical issue in the study of targeted drug delivery is the choice of carrier materials [19]. Successful targeted preparations should have three elements of targeted concentration, controlled release, and non-toxic and biodegradable. It can be called a successful targeting agent only if the target concentration can be set according to the patient's condition, the treatment method can be controlled release to cancer cells, and the implementation is non-toxic and biodegradable. The modified drug carrier is used as a "missile" to deliver anti-cancer drugs to the target area for concentration.

(1) PLA-PLL as carrier material

Polylactic acid (PLA) is a biodegradable material with good biocompatibility, non-toxic and harmless to the human body, and is currently one of the most commonly used synthetic biodegradable polymers in medicine. Polylactic acid can be prepared by polycondensation of lactic acid or ring-opening polymerization of lactide [20-21]. Lactic acid is a chiral molecule that exists in two isomeric forms, which can lead to four different forms of polymers: D-PLA, L-PLA, LEWIS-PLA, and meso-PLA.

However, because of the hydrophobicity of PLA, the problem of aggregation and inactivation of encapsulated peptide drugs has not been solved, and the end groups of PLA have fewer groups for connecting RGD sequence peptides, so only PLA is used as a targeted nanomaterial to inhibit tumor cells. Not ideal enough.

The cationic polymer poly-L-lysine PLL has good biocompatibility, and the degradation product is an essential amino acid for the human body. It has low immunogenicity and no toxic side effects, which is unmatched by other materials [22]. Its structure is flexible, stable, easy to adjust its molecular weight, polymer synthesis, polymer shape (The specific shape of the polymer is relatively random and the styles are diverse. Including linear, star, random network, block, graft, etc.), and it can be introduced by introducing side chains and specific targeting groups To modify the polymer backbone, and then adjust and improve the performance of the carrier, so the cationic polymer carrier has a larger space for development.

Combining PLA and PLL can take advantage of both. The poly-L-lysine complex is still positively charged and can bind to the negatively charged receptors on the cell surface, and is taken into the cell to achieve the purpose of targeting.

(2) RGD modified PLAL

With the continuous in-depth research of RGD sequence peptides on tumor therapy, people increasingly realize that choosing a suitable carrier as a target drug target is the key to successful tumor therapy.

The size of the PLA-PLL-RGD nanoparticle complex is about 50-500nm, and it has the characteristics of long circulation, recessiveness and three-dimensional stability in the body. These characteristics are conducive to drug targeting and are a good carrier for anti-tumor drugs [23]. Nanoparticles are positively charged. When the complex nanoparticles enter the body, they can overcome many obstacles in the process of reaching target cells, such as opsonins (serum antibodies, complement. These two opsonins are a method to measure the immune function of the body, and

are of great significance to the observation of the curative effect of breast cancer.), phagocytic system, extracellular matrix, degrading enzymes, etc. However, the surface of the composite nanoparticle is connected to the receptor specifically expressed on the cell surface to solve the targeting problem, so that the composite can pass through numerous obstacles and reach the target cell safely and without damage. Since the carrier material is biodegradable, the purpose of slow and controlled release can be achieved by adjusting the degradation rate of the carrier material [24-25].

2.3. The Effect of Exercise on the Quality of Life of Cancer Patients

Most diseases affect the patient's physical function. In the past, it was believed that patients with chronic diseases should rest and avoid physical activity. However, excessive rest and lack of physical activity may lead to "adaptation", which reduces the physiological function and quality of life. Current medicine advocates changing the concept and encouraging patients to take physical activity during the recovery period. It is now believed that exercise rehabilitation is an effective way to improve the physical and mental health of patients [26].

The rehabilitation of patients involved in exercise is a challenge, and exercise is based on the patient's motivation, ability and desire. Now, physical activity is usually recommended to people with heart disease and integrated into rehabilitation programs. The psychological, social and physical benefits of physical activity after myocardial infarction, coronary artery bypass grafting, heart transplantation, and stable congestive heart disease have been well documented. Exercise therapy is also incorporated into some common cancer treatments, which is of great significance and value. Physical activity also has a positive effect on clinically depressed patients. Although the physical and emotional damage of cancer patients is very serious, sports rehabilitation is still not a routine component of cancer treatment. In recent years, the field of sports rehabilitation among cancer patients has gradually attracted interest [27-28]. Some cancer patients perform certain rehabilitation exercises according to their individual physical conditions, which is considered to be one of the effective means for cancer patients to effectively improve the quality of life. Although some evidence shows that physical activity of cancer patients is generally beneficial, there is still a lack of understanding of the best type, duration, frequency and exercise cycle. Usually, the aerobic component of physical activity planning and health promotion has been emphasized. However, the method of over-emphasizing aerobic components may not be the most effective for cancer patients. Comprehensive exercise rehabilitation should be carried out. Appropriate strengthening of strength training is also beneficial to cancer patients. One of the most important goals of cancer patients is to improve quality of life (QOL). Therefore, it is important to understand the effects of different exercises at different stages of the disease and treatment of cancer patients.

(1) Exercise and immune system of healthy people

The human immune system is a highly complex system, which is produced by a large number of cell types and various cells of the immune system. That is, the various beneficial cells in the human body combine with each other to create a strong systemic organization. The whole function of the immune system is to remove malignant cells and pathogenic factors from the body. For cancer, natural killer cells, cytotoxic T cells and monocyte macrophage system are the main cells to recognize and kill tumor cells. About the effect of exercise on improving immune cells, many researchers have studied the changes of the number or activity of these cells before and after exercise.

NK cells are subpopulations of lymphocytes. They do not need major histocompatibility antigen complexes to recognize tumor cells and spontaneously produce cytotoxicity to tumors. Therefore, it

can be used as a first-line defense against tumor development. NK cells are very sensitive to exercise; under high-intensity exercise, their circulation number immediately increases by about 150-300%. After moderate intensity exercise, the cytotoxicity of NK cells also increased immediately, but there was no immunosuppression. With the regular exercise training, it was found that the population with sports history and excellent athletes significantly increased the cell activity of resting NK cells.

Cytotoxic T lymphocytes, like NK cells, have the function of killing tumor cells. However, unlike NK cells, they need tumor antigens expressed on primary histocompatibility antigen complexes. High intensity exercise increases the number by about 50-100%. Circulating cytotoxic T lymphocytes increase immediately after exercise, which may be induced by adrenaline. NK cells increased during exercise. Within 30 minutes after exercise, the number of circulating T lymphocytes increased significantly, which may be affected by adrenocortical hormone.

Monocyte macrophage system is the third type of cell which is important for the defense of tumor cells in vivo. Monocytes are produced from bone marrow, stored for a short time, then released into circulation, transferred to tissues or to fixed sites, where they mature into macrophages. Macrophages use their phagocytic, cytotoxic and cytotoxic abilities to play another anti-tumor role. This anti-tumor effect is able to gather some anti-cancer molecules to respond positively in the human immune system. In response to acute exercise, regardless of intensity and duration, the number of monocytes in peripheral blood increased instantaneously. However, the number of monocytes in acute moderate or high intensity exercise was not significantly different from that of peritoneal infiltration induced by inflammatory stimulation. In contrast, high-intensity exercise for several days may reduce the number of these cells by about 50%. Considering cell function, moderate exercise can increase phagocytosis and cytotoxicity of macrophages. At present, it is still unclear how exercise mediates the immune response of cytokines that regulate NK cell activity. It may be that tissue damage during exercise may cause monocytes and macrophages to secrete some cytokines.

(2) Exercise of cancer patients and tumor hypoxia

There is increasing evidence that hypoxia is prevalent in human tumors. Hypoxia, as one of the characteristics of malignant solid tumors, not only changes the biological characteristics of tumor cells, leading to genetic instability and malignant selection of tumor cells, but also one of the main reasons for tumor resistance to radiotherapy and chemotherapy. However, the mechanism of drug resistance induced by hypoxia is not very clear.

Under normal circumstances, oxygen supply in tissues can meet the metabolic needs of cells, but in tumor tissues, oxygen supply is often lower than the needs of cell growth and metabolism, resulting in hypoxia. The main reason of tumor hypoxia is the rapid proliferation of tumor cells. This hypoxia can also easily lead to the deterioration of the patient's condition. The rapid growth of tumor depends on the oxygen supply of the host blood vessels, but it is difficult to meet the needs of tumor cells, resulting in cell hypoxia. Hypoxia induces the growth of vascular endothelial growth factor VEGF, which initiates the angiogenesis of tumor itself. One of the essential features of tumor angiogenesis is angiogenesis. However, the structure of tumor blood vessels is abnormal. When the blood perfusion is insufficient, the blood vessels can not effectively produce compensatory reaction, which leads to the continuous existence of hypoxia in the tumor. Therefore, the continuous hypoxia of tumor can enhance the anaerobic glycolysis of tumor, increase the formation of new blood vessels, and promote the deterioration and metastasis of tumor.

In addition, the decrease of oxygen content can increase the resistance of tumor to radiation. Studies have shown that hypoxia can also reduce the radiosensitivity of almost all cells. However,

in the presence of oxygen, the radiosensitivity of tumor cells is significantly increased. This oxygen effect exists in all biological systems. The oxygen effect is that oxygen can react with the basic biochemical changes induced by radiation and affect the radiation effect. Free radicals generated during ionizing radiation cause various damages to living organisms. If oxygen is present, oxygen reacts with radical R to produce organic peroxide radicals.

Aerobic exercise not only promotes the oxygen supply of the body, but also promotes the oxygen supply of tumor tissue. On the one hand, it inhibits the rise of indexes that are positively related to the malignant degree of tumor, such as neovascularization, glycolysis, and the increase of Er - α level; on the other hand, and indicators such as tumor mutational burden, which are positively correlated with tumor malignancy, exercise promotes the oxygen supply of tumor, which provides the possibility for promoting the curative effect of radiotherapy and chemotherapy and improving the drug resistance of tumor to a certain extent.

3. Experimental Design of Exercise Against Breast Cancer Drug Loaded Nanoparticles Delivery System

3.1. Preparation of Drug Carrier Materials

In this study, the bioactive peptide RGD was grafted to PLL-PLA to form a PLL-PLA-RGD polymer, and mitoxantrone (DHAQ) was used as a model drug to prepare PLL-PLA-RGD drug-loaded nanoparticles, PLA-PLL- The size of RGD nanoparticle complex is about 50-500nm. This drug carrier material has strong adaptability to the human body. It has the characteristics of long circulation, recessiveness and three-dimensional stability in the body. These characteristics are conducive to drug targeting and are a good carrier for anti-tumor drugs. Nanoparticles are positively charged. When polymer nanoparticles enter the body, they can overcome many obstacles in the process of reaching target cells, such as opsonins (serum antibodies, complement), phagocytic system, extracellular matrix, degrading enzymes, etc.; at the same time RGD peptides are grafted onto the surface of polymer nanoparticles to solve the problem of active targeting, so that the polymer can pass through numerous obstacles and reach target cells safely and without damage. Because the carrier material is biodegradable; therefore, the drug can be released with the degradation of the carrier material to achieve the purpose of sustained release.

3.2. Experimental Animals and Cell Lines

60 female C57BL/6J mice, with an average weight of 15g, were purchased from the Animal Center of the Chinese Academy of Sciences.

The human breast cancer cell line BCAP-37 was purchased from the Institute of Cell Biology, Chinese Academy of Sciences.

Thirty female Balb/c nude mice aged 4-5 weeks were raised under SPF laboratory conditions. After adaptive support, the tumor is implanted under the skin. Two weeks after planting, the weight was 18.71±1.82g, 24 tumors were successfully planted, and then the exercise experiment was started with a volume of 0.054cm 3. Randomly divide into 4 groups, each with 6 animals. They are: blank control group A (no exercise, injection of saline); exercise group B (exercise, injection of saline); drug group C (no exercise, injection of nanoparticles); exercise + drug group D (exercise, injection of nanoparticles).

3.3. Experimental Sports Design

Nanoparticles were injected once a week, and the dosage was calculated as mitoxantrone hydrochloride 2mg/kg body weight. The mice in the blank control group A were administered with the tail vein and sacrificed 8 days after the injection of saline and medicine. Exercise group B mice were sacrificed 9 days after injection of saline and drugs. The mice in the drug group C began to exercise 24h after the injection of the drug. The exercise time variable is converted according to the exercise time required by the human body in scientific treatment, and the daily exercise time was 10min and 20min respectively.They exercised once a day and were sacrificed after 7 days of exercise; the mice in the exercise+drug group D began to exercise 48h after the injection, and they exercised every day. The time was 10min, 20min, exercise once a day, and executed 7 days later. Measure the length and short diameter of the tumor twice a week, and calculate the formula according to the tumor volume:

$$V = \frac{1}{2}ab^2 \tag{1}$$

V -volume, a -tumor long diameter, b -tumor short diameter, calculate the size of the tumor, and draw the tumor growth curve. The measurement of volume, long diameter and short diameter is very important for subsequent diagnosis and treatment. According to the tumor inhibition rate formula: tumor inhibition rate = (tumor model group average tumor volume-treatment group average tumor volume) / tumor model group average tumor volume, calculate the tumor inhibition rate of each group.

3.4. Statistical Analysis

The experimental results are all expressed as mean±standard deviation. Statistical analysis uses SPSS13.0 software to carry out the analysis of variance. The statistical significance is $P<0.05$, and the very significance is $P<0.01$.

4. Analysis of The Experimental Results of The Effects of Exercise and Drugs on Tumors

4.1. Changes of Drug Concentration in Breast Cancer Tissue of Mice After Exercise

After exercise, there was no significant difference in drug concentration of breast cancer tissue between 10 min-24 h exercise group and 10 min-48 h exercise group ($P > 0.05$), and there was no significant difference between 20 min-24 h exercise group and 20 min-48 h exercise group ($P > 0.05$). The details are shown in Table 1 and Figure 1.

Table 1. Drug concentration in mouse breast cancer tissue (ng/g) (n=8)

	24h	48h
Drug group	0.2993±0.06014	0.3077±0.06646
Exercise group 10min	0.3553±0.01350	0.3730±0.05761
Exercise group 20min	0.4440±0.04331	0.6340±0.13892

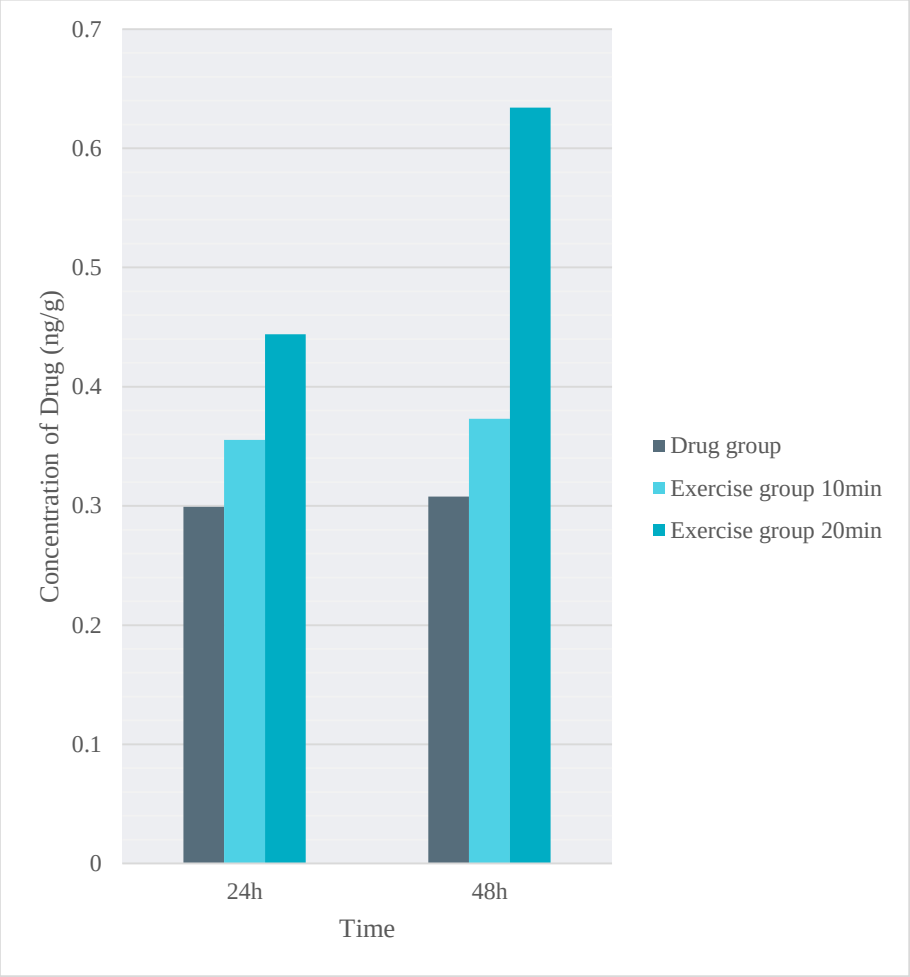

Figure 1. Drug concentration map of liver cancer tissue in the drug group, exercise 10min and exercise 20min group

It can be seen from Figure 1 that the drug concentration in breast cancer tissue of 20 min exercise group is significantly different from that of drug group ($P < 0.01$), and that of 20 min exercise group is significantly different from that of 10 min exercise group ($P < 0.05$); it can also be seen from figure 1 that the peak area of chromatogram of exercise 20 min is also larger than that of exercise 10 min and drug group. These results indicate that exercise can improve the targeting of drug loaded nanoparticles, and with the increase of exercise intensity, the targeting effect of drug loaded nanoparticles on breast cancer is enhanced. This also shows that the method proposed in this paper has certain utility in practical application. There was no significant difference in drug concentration between the 10 min exercise group and the drug group ($P > 0.05$), but the data showed an increasing trend. It suggested that exercise intensity is a very important factor to achieve the ideal target effect, but the specific exercise load threshold needs further research. The tumor growth trend of each group is shown in Figure 2.

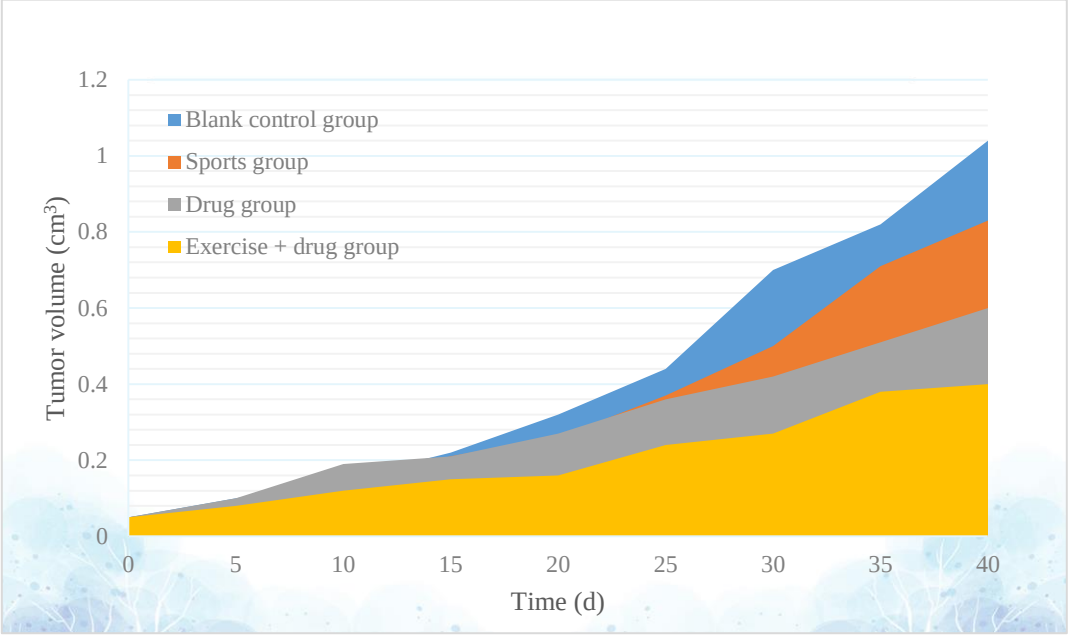

Figure 2. Tumor growth trend in each group

Compared with the tumor model group, the tumor volume of the exercise group was slightly smaller than that of the control group, with no statistically significant difference ($P > 0.05$); the tumor volume of the drug group was smaller than that of the tumor model group, the difference was significant ($P < 0.05$), but the difference was not statistically significant ($P > 0.05$); the tumor volume of the drug + exercise group was significantly different from that of the tumor model group ($P < 0.01$), and the difference was significant ($P < 0.05$), There was no significant difference between the two groups ($P > 0.05$).

4.2. Changes of NO Concentration in Breast Cancer Tissue of Mice after Exercise

After exercise, there was no significant difference in the concentration of no in breast cancer tissue between 10 min-24 h exercise group and 10 min-48 h exercise group ($P > 0.05$). Similarly, NO concentration in breast cancer tissue of 20 min-24 h group was not significantly different from that of 20 min-48 h group ($P > 0.05$); Compared with the normal saline group, the concentration of NO in breast cancer tissue of drug group was significantly different ($P < 0.05$), indicating that the concentration of no in breast cancer tissue was increased under the action of drug, indicating that the concentration of no in breast cancer tissue targeted by drug was related to the concentration of NO (as shown in Table 2 and Figure 3).

Table 2. NO content in mouse breast cancer tissue (μmol/gprot) (n=8)

	24h	48h
Saline group	1.0327±0.61694	0.7921±0.38049
Drug group	1.4802±0.99118	1.5125±0.85619
Exercise group 10min	2.0103±0.33347	2.3496±0.45840
Exercise group 20min	2.6122±1.21870	3.3744±1.01792

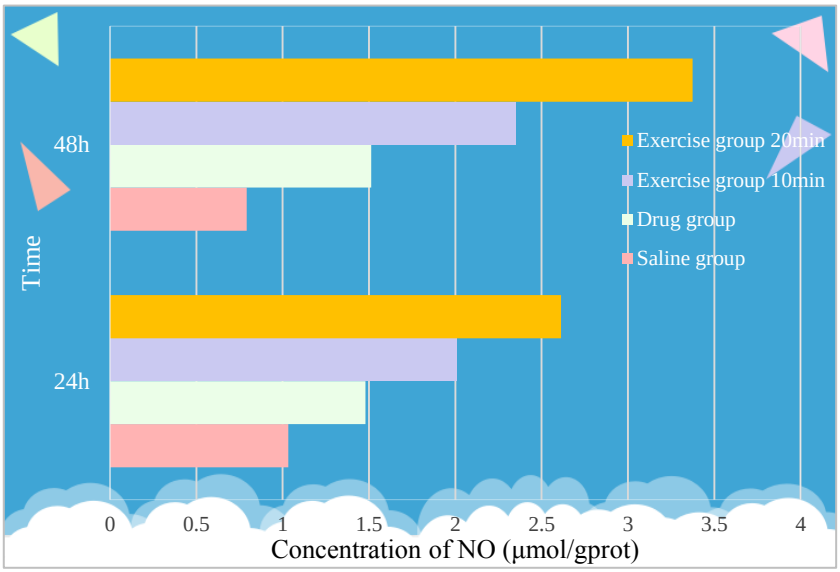

Figure 3. The NO content of the four groups of tumors

As can be seen from Figure 3, there is a significant difference in the concentration of NO in breast cancer tissue between the 10min exercise group and the drug group ($P<0.05$), and the S20 group has a very significant difference compared with the normal saline group ($P<0.01$). There is a significant difference in NO concentration between the 20-min exercise group and the 10-min exercise group ($P<0.05$), indicating that exercise at an appropriate intensity can increase the concentration of NO in breast cancer tissue; and as the exercise time increases, the concentration of NO It also increases correspondingly; the mechanism may be that exercise causes blood flow to increase, and the shear stress of blood to the blood vessel wall increases, which leads to increased NO synthesis.

Exercise can enhance the targeting of drug-loaded nanoparticles to breast cancer, and with the extension of exercise time, the targeting is also enhanced. There is a positive correlation between exercise, NO and the targeting of drug carriers. The mechanism may be that exercise causes an increase in NO concentration, and the increase in NO concentration causes an increase in αvβ3, and the drug carrier with RGD on the surface is related to The tumor tissue αvβ3 is combined to bring the drug-encapsulated carrier into the tumor tissue. Since the drug-encapsulated carrier is a biodegradable material, the drug can be slowly released in the tumor tissue as the material degrades, which can be used for a long time. The time to maintain the drug concentration and kill the tumor cells.

4.3. The Impact of Exercise on the Drug Targeting System

At present, drug targeting systems are a hot spot in pharmaceutical research. The targeting of drug carriers to tumors is a complex and multifactorial process; targeted drug delivery should not only target a certain organ, but also target diseased tissues, such as in the treatment of breast cancer, tumor drugs should not only make the drug concentration in the breast high, but also make the drug concentration in breast cancer cells, while the concentration in normal liver cells is not high; Drug targeting systems need to be effective in treating conditions without impairing liver function. And targeted drug delivery systems are used in tumor biotherapy, especially there is great potential for

development in solving the problem of tumor multidrug resistance. By modifying and grafting the bioactive peptide RGD on the surface, the surface characteristics of NP are changed, so that NP can escape the conditioning effect of plasma components and avoid being swallowed by the reticuloendothelial system. However, there are some problems in targeted drug delivery, such as the unstable carrier and the lack of recognition of tumor sites.

This study explores the relationship between exercise and targeting from the perspective of exercise, and studies the influence of moderate exercise on drug carrier targeting. The results showed that after a week of exercise, the 20-min exercise group had a very significant difference compared with the drug group ($P<0.01$), and the 20-min exercise group was also significantly different from the 10-min exercise group ($P<0.05$). And compared with the drug group, the drug concentration of tumor tissue in the 10min exercise group is not significantly different ($P>0.05$), but the concentration of tumor drug has a tendency to increase, which indicates that suitable exercise can increase the target of the drug targeting system. Tropism, and with the increase of exercise intensity, the targeting effect on breast cancer is enhanced. The specific data is shown in Figure 4.

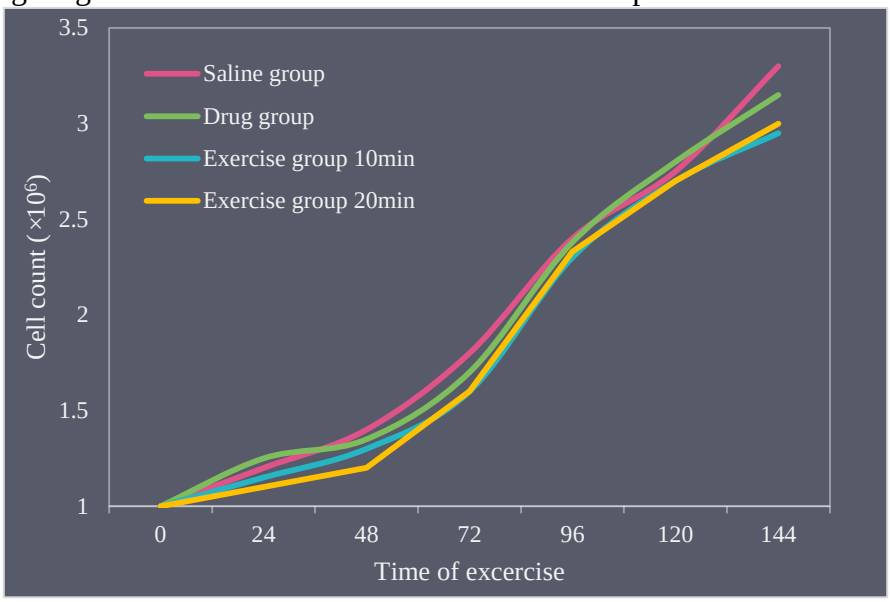

Figure 4. The influence curve of exercise on the drug targeting system

Exercise can promote the blood circulation of the body. It can indirectly promote the drug circulation to the tumor site, promote the targeting of targeted materials to tumor blood vessels, and indirectly promote the killing of tumor cells by anticancer drugs wrapped in targeted materials.

5. Conclusion

"Life lies in sports." Many studies have confirmed the prevention of exercise and the treatment of many diseases. No matter the effect is obvious or small, exercise has its own effect. Although exercise has been regarded as a taboo for cancer patients from the beginning, it has now been regarded as one of the important factors of breast cancer rehabilitation training, proving the value and development possibilities of exercise in the field of cancer rehabilitation training. This article is based on the study of the effect of sports on the curative effect of the drug-loaded nanoparticle drug delivery system against breast cancer. It is found that sports can assist the treatment of PLA-PLL-RGD nanoparticles and improve its curative effect. The combination of exercise and

PLA-PLL-RGD nanoparticles is better than pure PLA-PLL-RGD nanoparticles.

The nano-drug delivery system used in this study is polylactic acid-polylysine (PLAL) synthesized by the Tumor Targeting and New Drug Delivery System Laboratory of our City Cancer Institute, using arginine-glycine-aspartic acid (RGD). After modification, it has the characteristics of actively targeting the integrin αvβ3 expressed on tumor neovascularization, actively bringing the nanomedicine into the tumor site, and internalizing it into the tumor tissue and the tumor tissue space through cell phagocytosis, thereby reducing the toxic and side effects on healthy tissue.

This study found that sports can enhance the tumor tissue targeting of PLA-PLL-RGD nano drug delivery system. Sports increase the cytokines that kill tumor tissues. Several mechanisms are used to kill or inhibit the growth of tumors, indicating that exercise can be used as an adjuvant treatment for tumor patients during chemotherapy. Under appropriate exercise, breast cancer has high expression of NO and high drug concentration, and with the increase of exercise time, the drug concentration and NO concentration in breast cancer tissue increase, indicating that under the action of exercise, the increase the RGD-modified drug-loaded nanoparticles can target tumors and increase the concentration of tumor tissue drugs. However, the research on the role of RGD peptide in tumor treatment has just begun, and its detailed mechanism of action needs to be further studied. With the deepening of research on RGD peptide and oncology, RGD peptide will definitely play its unique role in tumor treatment, and its clinical application The breadth and depth will increase day by day.

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