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The Therapeutic Progress of Chemotherapy Drugs in Breast Cancer

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Abstract. Cancer is a health problem which is concerned by people. Recently, the mortality and incidence rate of breast cancer are significantly increasing. So far a variety of treatments for breast cancer have been developed, such as surgical therapy, radiotherapy and so on. But there are side effects during treatments, affecting patients' treatment effect and living. And chemotherapy drugs are more commonly used clinically, which are a common way to treat cancer. Therefore, the purpose of this paper is improving the side effects through summarizing the mechanism of action of chemotherapy drugs in treating breast cancer, collecting clinical data on chemotherapy drugs in treating breast cancer and analyzing the data. This article reveals that developing new chemotherapy drugs and adopting combination therapies can enhance the treatment effect of chemotherapy drugs and improve their side effect through introducing taxanes, anthracyclines, antimetabolites, microtubule inhibitors, and platinum compounds. However, chemotherapy drugs for breast cancer need further improvement. In the future combination therapies with chemotherapy drugs should be appropriately adopted according to patients' condition, and develop new chemotherapy drugs with fewer side effect providing support for the clinical treatment of breast cancer.

Keywords: breast cancer, chemotherapy drug, treatment

1. Introduction

Breast cancer is a tumor with highest female incidence, affecting women's physical health, living quality and psychological state. According to statistics, the incidence of female breast cancer in China ranks second among tumors, and the mortality rate is 10,5/100,000. In 2020, the incidence of female breast cancer has exceeded lung cancer, meaning that breast cancer has become the most common cancers [1]. There are many factors which can lead to breast cancer, such as genetic factors, obesity, lifestyle and so on. Genetic factors are one of the causes of breast cancer, the risk of breast cancer will be significantly increased if there is breast cancer genetic gene in the family. According to the statistics, overweight persons have a 15% higher risk of breast cancer, and obese individuals have a 34% higher risk of breast cancer. Unhealthy lifestyles such as smoking also increase the risk of breast cancer [2]. According to research, there is a positive correlation between the risk of breast cancer and smoking. The ways to treat breast cancer include surgical treatment, Radiotherapy and chemotherapy. Surgical treatment can eradicate the lesion, but it is more difficult to treat breast cancer once it recurs or metastasizes to other parts. Radiotherapy can reduce the

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treatment time, but patients will have adverse reactions during radiotherapy such as nausea, vomiting, diarrhea and hair loss. And chemotherapy can increase the cure rate of patients. Nowadays, a variety of chemotherapy drugs for the treatment in breast cancer have been developed such as taxane drugs, anthracycline drugs, antimetabolite drugs, microtubule inhibitor drugs and platinum drugs, which are the first-line clinical drugs and widely used. However, chemotherapy drugs can cause side effects due to their inherent toxicity, which can make the treatment process difficult and affect the treatment effect of patients. In view of this, this paper will summarize and generalize the treatment mechanism, clinical effect and commonly used chemotherapy drugs at present, in order to provide research value for the research and development of new chemotherapy drugs.

2. Breast cancer

Breast cancer is a malignant tumor which formed by abnormal cell proliferation in breast tissue, mainly occurring in breast ducts or lobules. Breast cancer is a tumor with high incidence and mortality rates among women, and men can also develop breast cancer, the probability is very low. According to statistics, by 2040, breast cancer's the incidence and mortality rates in Asia can rise to the top globally. In China, the incidence rate of breast cancer among urban women is higher than that in rural areas. The incidence and mortality rates of breast cancer of Chinese women aged 30-54 rank first among all types of cancer. And there is a positive relation between the incidence and mortality rates and age: the highest incidence rate of breast cancer occurs in women who aged 60-64, and the highest mortality rate occurs in women who aged 70 and above. The most typical clinical manifestation is a breast lump. In the early stage of breast cancer, it can cause enlargement of axillary lymph nodes on the same side with movable induration, and as the disease progresses, the lymph nodes will fix to the surrounding skin tissue. In advanced stages, enlarged lymph nodes can be caused by the supraclavicular and contralateral axillae. The mechanisms of chemotherapy drugs in treating breast cancer include regulating the cell cycle, affecting DNA synthesis of breast cancer cells, promoting tumor cell apoptosis, inhibiting microtubule depolymerization, and suppressing breast cancer cell metastasis. Currently, the main progressions are the development of novel chemotherapy drugs and combination treatments.

Currently, breast cancer therapies still faces many challenges: early-stage breast cancer can spread without being detected, and it may recur 5 to 10 years after surgery. Tumor cells may also metastasize, such as brain metastasis and bone metastasis: after brain metastasis, the blood-brain barrier will restrict drug penetration, and after bone metastasis, targeting RANKL can reduce bone-related events, but can't achieve a cure. During the treatment, patients may produce resistance to chemotherapy drugs, reducing their effectiveness and affecting the treatment progress. The difficulty in treating triple-negative breast cancer is the lack of targets, making it impossible to use targeted drugs. Currently, chemotherapy is mainly relied on treatment. But, during chemotherapy, the drugs can cause toxicity to all body cells, leading to adverse reactions such as bone marrow suppression, cardiotoxicity, and neurotoxicity, which seriously affect the treatment outcome and quality of life of patients.

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3. Common chemotherapy drugs for breast cancer and their mechanisms of action

3.1. Taxanes

The most typical taxane drug is paclitaxel. Paclitaxel was originally a chemical substance extracted from the bark of the Pacific yew tree. However, extracting paclitaxel requires cutting down 3,000 century-old yew trees, which can lead to an ecological crisis. So, people usually produce it through plant cell culture technology or semi-synthesis. Paclitaxel can bind to microtubule proteins and inhibit microtubule depolymerization, thereby blocking the tumor cell cycle. Paclitaxel can play a role in adjuvant chemotherapy in the early stages of breast cancer, significantly improving the rate of complete pathological response. In advanced breast cancer, paclitaxel can be used in combination with bevacizumab to extend patient survival. Clinical data show that the efficacy rate of paclitaxel in treating breast cancer is 34%, and the disease control rate is 48% [3]. However, paclitaxel is insoluble in water, and it needs to be dissolved in anhydrous ethanol and polyoxyethylene castor oil to help dissolve. Polyoxyethylene and castor oil can cause allergic reactions, which can aggravate peripheral neurotoxicity in breast cancer patients during clinical treatment, leading to allergic reactions and affecting the treatment outcome. The latest taxane chemotherapeutic drugs are albumin-bound paclitaxel and polymeric micellar paclitaxel. The mechanism of albumin binding is similar to that of paclitaxel. Still, its solubility is better than that of paclitaxel. It doesn't need to use other chemicals as solvents, reducing the risk of causing allergic reactions in patients, and albumin-bound paclitaxel has a high tumor delivery rate; it doesn't need to use hormone pretreatment before delivery. Albumin-bound paclitaxel improves the poor solubility of paclitaxel in clinical treatment, reduces the side effects caused by castor oil during treatment, and increases the cure rate of patients. Clinical data show that the overall efficacy rate of albumin-bound paclitaxel in treating breast cancer is 45.8%, the disease control rate is 73.7%, and the adverse reactions are mild; the efficacy rate of polymeric micellar paclitaxel is 43.5%, the disease control rate is 85.4%, the median progression-free survival (PFS) is 9 months, the incidence of allergic reactions is 0%, the incidence of neuropathy is 9.8%, and the incidence of neutropenia is 22% [4]. Currently, paclitaxel still poses risks of neurotoxicity and allergy. In future research, the structure of paclitaxel can be modified to improve its solubility and reduce the risk of allergic reactions in patients.

3.2. Anthracene class

Among anthracyclines, doxorubicin is a representative drug. The chemical substance which initially isolated from Streptomyces by people is called daunorubicin, which is chemically modified to obtain doxorubicin, which is found to have stronger activity against solid tumors. Nowadays, chemical modification or fermentation can be used for production. Doxorubicin can activate the signaling pathway of p53, upregulate spermidine spermine N1-acetyltransferase 1 and arachidonic acid oxygenase 15, promoting lipid peroxidation and ferroptosis. In the early treatment, doxorubicin can be used in combination with cyclophosphamide to alleviate patients' symptoms. In advanced treatment, doxorubicin can combine with trastuzumab to improve the condition of breast cancer patients. Clinical data show that the efficacy of doxorubicin in treating breast cancer is 36%, and the disease control rate is 58% [5]. However, studies show that doxorubicin can cause left ventricular dysfunction, arrhythmia, myocardial injury and so on. This means that every breast cancer patient who is treated with doxorubicin may become a heart disease patient, and treatment may be interrupted due to the occurrence of cardiotoxicity. Currently, the novel chemotherapeutic drug liposomal doxorubicin which is a nanoscale drug carrier, can increase the accumulation of drugs in

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tumor tissues and reduce the accumulation of free doxorubicin in the heart, reducing the risk of doxorubicin damaging myocardial cells during treatment. The incidence of cardiotoxicity in breast cancer patients treated with liposomal doxorubicin is 4.7%, and the incidence of traditional doxorubicin is 21% [6]. The combination of liposomal doxorubicin and doxorubicin greatly reduces the probability of the development of heart disease of breast cancer patients and improves their survival rate. In addition, antibody-conjugated doxorubicin, as a targeted drug, can significantly enhance efficacy and reduce systemic toxicity. The efficacy rate in treating breast cancer is 60.9%, the disease inhibition rate is 97.3%, and the median progression-free survival (PFS) is 16.4 months, which is better than traditional doxorubicin, making patients have a higher quality of life [7]. Currently, the impact of anthracyclines on the heart remains an obstacle in the treatment of breast cancer. In future research, by reducing the cardiotoxicity of anthracyclines or combining them with other non-toxic substances, the cardiotoxicity of anthracyclines used alone can be attenuated, reducing the risk of myocardial cell damage.

3.3. Anti-metabolite class

Among antimetabolite drugs, 5-fluorouracil is a typical example. 5-fluorouracil is developed based on chemical modification of uracil molecules. The initial design idea was to synthesize fluorinated uracil, which selectively kills cancer cells by interfering with DNA/RNA synthesis. 5-fluorouracil can activate caspase-3 and caspase-9 by inducing the production of reactive oxygen species (ROS) and the mitochondrial pathway, inducing apoptosis in cells. In the early treatment, 5-fluorouracil can be used in combination with methotrexate and cyclophosphamide to reduce the recurrence rate of breast cancer. The response rate of 5-fluorouracil in the treatment of breast cancer is 14%, and the disease control rate is 32%. However, studies have shown that 5-fluorouracil can cause bone marrow suppression, leading to a decrease in white blood cells and platelets. Patients may experience anemia during treatment, increasing the risk of bleeding and infection. Additionally, 5-fluorouracil can also cause hand-foot syndrome, which patients may experience peeling, ulceration, and painful erythema on the palms and soles of their feet, posing significant challenges to treatment. Liposomal 5-fluorouracil can reduce the systemic toxicity of 5-fluorouracil by targeted delivery, decreasing the incidence of bone marrow suppression and hand-foot syndrome, alleviating the pain and improving the cure rate for breast cancer patients during treatment. The response rate of liposomal treatment for breast cancer is 15% to 25%, and the disease control rate is 40% to 50%. The incidence of neutropenia in bone marrow suppression is 12.5%, and the probability of thrombocytopenia is 8.3%. The incidence of hand-foot syndrome is 25% [8]. 5-fluorouracil can also be used in combination with pembrolizumab, elevating the response rate to 53% and the disease control rate to 79%. It is also effective for patients with visceral and brain metastases. Currently, the strong side effects of 5-fluorouracil significantly reduce the success rate of breast cancer treatment, reduce the quality of life, and affect their treatment effect. In future research, combining 5-fluorouracil with other substances to create targeting properties can attenuate the systemic toxicity of 5-fluorouracil and reduce its damage to other tissues in the patient's body.

3.4. Microtubule inhibitors

Among microtubule-inhibiting chemotherapeutic drugs, eribulin is a typical example. Eribulin was initially developed from sea hare toxin, but due to its extremely low content, a simplified derivative of sea hare toxin, eribulin, has been developed by chemical synthesis. Eribulin can bind to the plus ends of microtubules in breast cancer cells, inhibiting microtubule growth in interphase cells,

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Leading to tubulin polymer storaged as nonproductive aggregates , arresting the cell cycle in G2/M phase, and blocking the tumor cell cycle to induce apoptosis. In the treatment of advanced breast cancer, eribulin has shown good efficacy in metastatic breast cancer, improving patients' quality of life and prolonging their survival. The response rate of eribulin in breast cancer treatment is 12.2%, and the disease control rate is 46.6%. However, eribulin has significant side effects such as peripheral neuropathy, numbness or tingling in hands and feet. The combination of eribulin and gemcitabine for breast cancer treatment has higher efficacy and safety compared to eribulin alone. When eribulin and gemcitabine are used in combination for breast cancer treatment, the disease control rate is 65%. The combination of eribulin and gemcitabine improves the disease control rate and is particularly effective for patients with triple-negative breast cancer. Eribulin can also be used in combination with durvalumab for breast cancer treatment, with an efficacy rate of 26% and a disease control rate of 54%. It is also effective for patients with visceral metastasis and chemotherapy resistance [9]. Currently, due to its strong and relatively uncontrollable side effects, it pose a significant risk. In future research, chemotherapy drugs with less toxicity or side effects should be used as alternatives to eribulin. Alternatively, combination therapy methods can be employed to synergize eribulin with other chemicals, reducing the risk of side effects caused by eribulin's toxicity when used alone, and providing safeguards for the clinical treatment of breast cancer.

3.5. Agents

Among platinum drugs, cisplatin is a typical representative. Cisplatin is a compound which is produced during the electrolysis of platinum electrodes. In the early treatment, cisplatin combined with paclitaxel can be effective. In the advanced treatment of, cisplatin combined with gemcitabine can prolong the survival of patients. The main biological target of cisplatin is genomic DNA, which can cause significant DNA damage, blocking the transcription and replication of tumor cells. The response rate of cisplatin in breast cancer treatment is 23%, and the disease control rate is 56%. However, if these DNA damages are not properly repaired or treated, they can strongly induce the death of other normal cells. The toxicity of sapcitabine is lower than that of cisplatin, reducing the adverse reactions in breast cancer patients during treatment. Moreover, sapcitabine is an oral agent, avoiding the inconvenience of intravenous injection and improving the medication convenience and quality of life for patients. The nephrotoxicity of sapcitabine is 10% to 15%, and the nephrotoxicity of cisplatin is 20% to 30%. The probability of neuropathy with sapcitabine is 5% to 8%, and the probability of cisplatin is10%. Therefore, sapcitabine is safer than cisplatin in treatment. Lobaplatin, as a third-generation platinum derivative, has the characteristics of high efficacy and low toxicity. The response rate in breast cancer treatment is 23.8%, the disease control rate is 57.9%, and the median progression-free survival (PFS) is 4.2 months, reducing the side effects during treatment and increasing the therapeutic effect for patients [10]. Currently, cisplatin still causes damage to other cells, posing certain risks in clinical treatment. However, sapcitabine and lobaplatin have relatively low nephrotoxicity and neurotoxicity, and are convenient to take, improving the convenience of treatment and the quality of life in clinical practice.

4. Challenges and prospects

In the treatment of breast cancer with chemotherapy drugs, there are many challenges. During the treatment process, adverse reactions such as drug resistance, bone marrow suppression, cardiotoxicity, neurotoxicity, nausea, and vomiting may occur, which vary from patient to patient.

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Therefore, appropriate treatment methods and chemotherapy drugs need to be used based on the actual situation of each patient. These adverse reactions have not been completely avoided to date, exacerbating patients' pain during treatment and affecting their treatment outcomes and quality of life. Although these side effects cannot be completely avoided, they can be improved through various approaches. For chemotherapy drugs that require the addition of other compounds during use, people can combine them with other substances to change their properties, making it unnecessary to add other compounds during use. For highly toxic chemotherapy drugs, people can replace traditional chemotherapy drugs with less toxic drugs or combine chemotherapy drugs with other substances to reduce the toxicity produced when the drugs are used alone. For chemotherapy drugs with systemic side effects, people can use targeted drugs to reduce the attack on systemic cells and alleviate patients' adverse reactions. For drugs with unavoidable side effects, people should monitor patients' conditions in real time and use drugs reasonably based on their actual situations to reduce adverse reactions or change the treatment method. With the continuous development of technology, people can also develop more novel chemotherapy drugs to provide support for the clinical treatment of breast cancer.

5. Conclusion

Currently, people have made certain progress in the breast cancer treatment, developing many chemotherapy drugs such as taxanes, anthracyclines, antimetabolites, microtubule inhibitors, and platinum drugs. Many mechanisms of action have also been studied, including inhibiting breast cancer cell proliferation, suppressing breast cancer cell metastasis, promoting cell apoptosis, and inhibiting microtubule depolymerization. This has led to significant treatment outcomes for some breast cancer patients and improved their quality of life. However, chemotherapy drugs still has many side effects, such as drug resistance, bone marrow suppression, nausea, and vomiting in patients. To reduce the side effects of chemotherapy drugs, people should replace traditional chemotherapy drugs with less toxic new drugs or develop new combination chemotherapy drugs to reduce the toxicity caused by the use of individual drugs. People can also develop new chemotherapy drugs specifically for breast cancer treatment, and tailor treatment methods to individual patients' conditions. It is hoped that this article can provide research value for the development of chemotherapy drugs and offer strong support for the treatment of breast cancer.

References

[1] Sung, H., Ferlay, J., Siegel, R.L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians, 71, 209 - 249.

[2] Bodelon, C., Sung, H., Mitchell, E. L., Deubler, E. L., Newton, C. C., Jemal, A., Teras, L. R., & Patel, A. V. (2024). Excess Body Weight and the Risk of Second Primary Cancers Among Cancer Survivors.JAMA network open, 7(9), e2433132.

[3] Sledge, G. W., Neuberg, D., Bernardo, P., Ingle, J. N., Martino, S., Rowinsky, E. K., & Wood, W. C. (2003). Phase III trial of doxorubicin, paclitaxel, and the combination of doxorubicin and paclitaxel as front-line chemotherapy for metastatic breast cancer: an intergroup trial (E1193). Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 21(4), 588–592.

[4] Kim, T. Y., Kim, D. W., Chung, J. Y., Shin, S. G., Kim, S. C., Heo, D. S., Kim, N. K., & Bang, Y. J. (2004). Phase I and pharmacokinetic study of Genexol-PM, a cremophor-free, polymeric micelle-formulated paclitaxel, in patients with advanced malignancies. Clinical cancer research : an official journal of the American Association for Cancer Research, 10(11), 3708–3716.

[5] Berry, D. A., Broadwater, G., Klein, J. P., Antman, K., Aisner, J., Bitran, J., Costanza, M., Freytes, C. O., Stadtmauer, E., Gale, R. P., Henderson, I. C., Lazarus, H. M., McCarthy, P. L., Jr, Norton, L., Parnes, H., Pecora, A.,

DOI: 10.54254/2753-8818/2025.AU27836

Perry, M. C., Rowlings, P., Spitzer, G., & Horowitz, M. M. (2002). High-dose versus standard chemotherapy in metastatic breast cancer: comparison of Cancer and Leukemia Group B trials with data from the Autologous Blood and Marrow Transplant Registry. Journal of clinical oncology : official journal of the American Society of Clinical Oncology, 20(3), 743–750.

[6] Modi, S., Saura, C., Yamashita, T., Park, Y. H., Kim, S. B., Tamura, K., Andre, F., Iwata, H., Ito, Y., Tsurutani, J., Sohn, J., Denduluri, N., Perrin, C., Aogi, K., Tokunaga, E., Im, S. A., Lee, K. S., Hurvitz, S. A., Cortes, J., Lee, C., … DESTINY-Breast01 Investigators (2020). Trastuzumab Deruxtecan in Previously Treated HER2-Positive Breast Cancer. The New England journal of medicine, 382(7), 610–621.

[7] O'Brien, M. E., Wigler, N., Inbar, M., Rosso, R., Grischke, E., Santoro, A., Catane, R., Kieback, D. G., Tomczak, P., Ackland, S. P., Orlandi, F., Mellars, L., Alland, L., Tendler, C., & CAELYX Breast Cancer Study Group (2004). Reduced cardiotoxicity and comparable efficacy in a phase III trial of pegylated liposomal doxorubicin HCl (CAELYX/Doxil) versus conventional doxorubicin for first-line treatment of metastatic breast cancer. Annals of oncology : official journal of the European Society for Medical Oncology, 15(3), 440–449.

[8] Udofot, O., Affram, K., Israel, B., & Agyare, E. (2015). Cytotoxicity of 5-fluorouracil-loaded pH-sensitive liposomal nanoparticles in colorectal cancer cell lines. Integrative cancer science and therapeutics, 2(5), 245–252.

[9] Pellegrino, B., Cavanna, L., Boggiani, D., Zamagni, C., Frassoldati, A., Schirone, A., Caldara, A., Rocca, A., Gori, S., Piacentini, F., Berardi, R., Brandes, A. A., Foglietta, J., Villa, F., Todeschini, R., Tognetto, M., Naldi, N., Bortesi, B., Montemurro, F., Ardizzoni, A., … Musolino, A. (2021). Phase II study of eribulin in combination with gemcitabine for the treatment of patients with locally advanced or metastatic triple negative breast cancer (ERIGE trial). Clinical and pharmacogenetic results on behalf of the Gruppo Oncologico Italiano di Ricerca Clinica (GOIRC). ESMO open, 6(1), 100019.

[10] Otsuka Tomoyuki, Nojiri Takashi, Minami Seigo, Hosoda Hiroshi, Kuroyama Muneyoshi, Hirata Haruhiko... & Kijima Takashi. (2017). Evaluation of Natriuretic Peptide in Non-small Cell Lung Cancer Patients Treated with Bevacizumab Together with Carboplatin-Paclitaxel: A Prospective Study..Anticancer research, 37(7), 3505-3512.