

Comparison of Traditional Treatments and Therapeutic Vaccines for Breast Cancer

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Abstract. One prevalent malignant tumor that poses a major risk to women's health is breast cancer. In addition, breast cancer is also one of the main causes of female mortality. Despite this, most breast cancer still uses traditional treatment, including surgery, chemotherapy, radiotherapy, etc. Although traditional treatment can control the disease process, there are a series of problems and limitations. Thus, there is an urgent need for novel therapies to improve the prognosis and the standard of living for those with breast cancer. Immunotherapy, as an innovative method of treatment, is receiving increasing attention. Cancer immunotherapy works by using the immune system's defenses to stop cancer from spreading and eradicate cancerous cells. Therapeutic vaccines are a highly anticipated immunotherapy. The unique advantages of therapeutic vaccines may become one of the main directions for cancer treatment. However, there are still many problems and challenges with cancer therapeutic vaccines at present. This review aims to discuss the advantages and research progress of therapeutic vaccines for breast cancer and discuss the potential and challenges of vaccines in the treatment of breast cancer. It aims to provide reference and guidance for further research on therapeutic vaccines against breast cancer.

Keywords: Therapeutic vaccine; breast cancer; immunotherapy.

1. Introduction

Breast cancer is a type of frequently malignant tumor. The health of women is seriously threatened by breast cancer. Three categories can be distinguished by breast cancer: BC-expressing hormone receptors, BC-expressing HER2, and triple-negative breast cancer [1]. Furthermore, the primary cause of death for women is breast cancer. It was projected that 2.26 million instances of breast cancer were reported in 2020 alone. [2].

Though most breast cancer still uses traditional treatment, including surgery, chemotherapy, radiotherapy, etc., although traditional treatment could kindly control illness processing, there exists a series of problems and limitations. To illustrate it, chemotherapy and radiotherapy would cause significant damage to patients' health. For example, surgery treatment might bring some contraindications and positive pathologic margins after lumpectomy [3]. Meanwhile, chemotherapy and radiotherapy also easily incur drug tolerance and relapse. Thus, there is a dear need for new treatment to improve breast cancer patients' survival rate and life quality.

Immunotherapy, as a new treatment, has received more and more attention. Cancer immunotherapy limits the growth of cancer and eliminates cancerous cells by utilizing the immune system's reaction. Immunotherapy has many types including CAR-T, immune checkpoint inhibitors, monoclonal antibodies, and cancer vaccine. Immunotherapy has unique benefits and potency through mediating patients' self-immune system to attack and clean cancer cells. Past research has shown immunotherapy is effective in triple-negative breast cancer. Therefore, multiple immunotherapies were also tested ongoing, including checkpoint inhibitors, antibodies, and vaccines. [4] In the breast cancer field, therapeutic vaccines received high attention as a type of therapy. A therapeutic vaccination for breast cancer may stimulate a patient's immune system to identify and combat cancer cells in order to have a therapeutic effect.

Breast cancer therapeutic vaccine research is still in its early stages, despite the fact that therapeutic vaccines are a prominent area of study and would play a significant role in cancer treatment. Meanwhile, there still exists many problems and challenges. Firstly, specific antigens are essential

for vaccine design. An ideal antigen could lead to a strong and broad T-cell response. However, it is still a problem to find and select the finer antigens. Another challenge is vaccine vectors identify is hard. A good vector should accurately deliver antigens to the cancer site. Otherwise, it is also necessary to consider whether the antigen and vector are suitable. Overall, the choice of antigens and vectors has become a key challenge for cancer vaccines [5]. Moreover, the design and selection of breast cancer vaccines confront certain difficulties because of the large heterogeneity of breast cancer. Therefore, further research and studies are needed to improve the efficacy and reliability of therapeutic vaccines for breast cancer.

This review is aimed at reviewing the progress of research on breast cancer therapeutic vaccines. In addition, it discusses the vaccine's potency and challenges in breast cancer treatment. First would compare traditional treatment and therapeutic vaccine. Including the limitations of traditional treatment and its reasons. Moreover, there are advantages of therapeutic vaccine over current treatment. Then, this paper will illustrate the application of therapeutic vaccines in breast cancer and other cancers, including the therapeutic vaccine's mechanism and target point, showing clinic efficiency of existing therapeutic vaccine products, stating therapeutic vaccine's current problems and technical difficulties, and the end, outlooking future application of therapeutic vaccine in breast cancer. Aiming could provide a reference and guide for further research on breast cancer therapeutic vaccines.

2. Traditional treatments and therapeutic vaccines

2.1. Limitation of current treatments and reasons

2.1.1. Chemotherapy

Chemotherapy usually uses drug to cure cancer. Chemotherapy through killing cancer cell, blocking growth of blood vessels, inhibiting cancer cell transfer and other pathway to cure cancer. Chemotherapy drugs usually kill cancer cells by killing rapidly dividing cells, but they also affect the division and growth of normal cells. Thus, producing a series of adverse reactions. As a result, a series of adverse reactions will occur. Such as nausea, vomiting, hair loss, oral ulcers, indigestion, skin sensitivity, etc. These side effects seriously affect patients' quality of life. Sometimes side effects can even cause patients to discontinue treatment [6]. Moreover, the heterogeneity of cancer cells means that different cancer cells may respond differently to the same chemotherapy drug. For instance, some cancer cells may be drug-resistant, resulting in poor treatment efficacy. To improve it, breast cancer is heterogenetic. It has multiple subtypes [3]. Therefore, the efficacy of chemotherapy is unideal on occasion.

2.1.2. Radiotherapy

Radiotherapy uses high-energy radiation to lead to DNA damage, cell apoptosis, microvascular damage. These results can lead to cancer cell death or inhibited growth to treat the cancer.

Radiotherapy not only affects tumor tissue but also affects surrounding normal tissue. Therefore, some side effects may occur, such as skin pain, fatigue, difficulty breathing, heart damage, etc [1]. These side effects may not directly threaten patients' lives but often affect their confidence in treatment.

2.1.3. Surgery

Surgery is one of the main treatments for breast cancer. Surgery removes cancer cells as completely as possible by removing tumor tissue from the breast. However, such surgeries are often not thorough in clearing cancer cells. Radiotherapy and chemotherapy still need to be coordinated after surgery to ensure the therapeutic effect. Obviously, surgery may require the removal of some or all the breast tissue [3]. Such changes in a patient's appearance and body shape may cause psychological and emotional distress to the patient.

2.2. Benefits of Therapeutic Vaccine

Compared to traditional therapies, therapeutic vaccines have the advantages of specific treatment and stimulating the immune system to participate in treatment. Tumor-specific antigens or specific proteins on the outer layer of cells with cancer in patients can be the focus of therapeutic vaccinations. As a result, it kills cancer cells specifically without harming healthy cells [7]. This specific treatment can reduce the side effects and improve the safety of the treatment. Therapeutic vaccines activate the the immunological system of the patient, induce a specific immune response, and enhance the capacity of the immune system to recognize and attack tumors. Compared to traditional therapies that directly kill tumor cells, therapeutic vaccines can trigger long-lasting immune memory in the body, preventing tumor recurrence and metastasis. Moreover, with the research and development in the past decade, therapeutic vaccines have become one of the frontier fields in cancer treatment, achieving some encouraging clinical trial results [8]. Despite facing some challenges and limitations, therapeutic vaccines, as an emerging treatment method, have good therapeutic prospects and bring new hope to cancer patients.

3. Vaccination for Breast Cancer

3.1. Mechanism and Different Targets

The essential principle of therapeutic cancer vaccine is that some antigens or epitope specifically express in cancer cell. Immune system could be induced by these antigens to activate immune cells [9]. Usually, classifying therapeutic cancer vaccine into 3 type, nucleic acid vaccine, protein vaccine, cellular vaccine. The mechanism of these 3 vaccines is different. Nucleic acid vaccine with the help of vector deliver nucleic acid into body. Nucleic acid is taken up by cell and translated into antigenic protein. These specifically antigenic proteins would be recognized and induce immune response. Effector T cell would kill cancer cell. Protein vaccine produce by synthetic long peptide. These synthetic long peptides would be injected into patients. Using synthetic long peptide could avoid immune tolerance and enhance CD4 and CD8 T-cell response. Cellular vaccine is different with other two types. Cellular vaccine needs isolate patient's dendritic cells. Then activate patient's dendritic cells in vitro. Whereafter, reinject these activated dendritic cells. Activated dendritic cells would induce immune response to kill cancer cells [9]. In conclusion, all types of cancer vaccine goals are the same. They all want to achieve antigen presentation and induce T-cell to kill cancer cells.

3.2. Current Products and Clinical Data

For therapeutic cancer vaccine, FDA have approve 3 products to sale [10]. Numerous cancer vaccines are likewise undergoing clinical trials at this time.

Talimogene laherparepvec (T-VEC; tradename IMLYGIC) was received approval in 2015. It is the newest cancer vaccine be approved. T-VEC is a vaccine against melanoma cancer. It is product base on herpes simplex virus (HSV). Meanwhile, inserting GM-CSF gene and delict 2 gene of infect cell protein [11]. T-VEC's effectiveness was confirmed in its 2019 final report. Treatment group's durable response rate (DRR) and overall response rate (ORR) are significant higher than control group. It was 50 patients get complete response in treatment group and only 1 patient get complete response in control group. And its side effects are acceptable including fatigue, chills, fevered. This remarkable result lead researchers do other further studies. Recently, some T-VEC monotherapy tests show it have safety profile and other benefits [11].

Even through there is no breast cancer therapeutic vaccine received approval, it still lot of breast cancer vaccine remain in clinical trial. NeuVax had gotten into phase 3 clinical trial (NCT01479244). However, it still was terminated because of its low efficiency. In breast cancer tissue, HER2 have characteristic expression. Thus, lot of breast cancer vaccine use HER2 as their target.

3.3. Comparison of Advantages and Disadvantages

Therapeutic vaccines have some advantages over traditional therapies. Therapeutic vaccines can achieve specific treatment by targeting specific tumor antigens and achieving specific killing of cancer cells. This specific killing of cancer cells reduces damage to normal tissues. In addition, therapeutic vaccines form long-lasting immune memory in the body. Immune memory can prevent tumor recurrence and metastasis, improve treatment persistence and efficacy. However, therapeutic vaccines also have some disadvantages. Therapeutic vaccines still face the problem of unstable therapeutic effects. Some patients may not achieve ideal treatment outcomes. In addition, the safety and tolerability of therapeutic vaccines still need further verification. To sum up, therapeutic vaccines for breast cancer have certain potential and advantages in the treatment of breast cancer, but further clinical research and verification are still needed to improve the efficacy and safety of treatment.

4. Conclusion

In this review, a comparison was made between traditional therapy and therapeutic vaccines. Explained the limitations and reasons of traditional treatment. Chemotherapy treats cancer by killing cancer cells, blocking the growth of blood vessels and inhibiting the spread of cancer cells. Nevertheless, a series side effect would happened include nauseas, vomiting, hair loss, etc. Moreover, these side effects would also affect the life quality of patients. Radiotherapy is used to treat cancer by high-energy radiation that causes DNA damage and cell apoptosis. However, radiotherapy would also impact normal surrounding tissue. Surgery is often followed by radiotherapy and chemotherapy and may cause changes in the patient's appearance and physical form, causing psychological and emotional distress. With the deepening of cancer research, immunotherapy methods have emerged. In this review, therapeutic vaccines were introduced as a type of immunotherapy method. The advantages of therapeutic vaccines over traditional treatments were illustrated. The benefit of therapeutic vaccines is that therapeutic vaccines are more specific than traditional treatment in treat cancer. Moreover, therapeutic vaccine could stimulate the immune system to participate in treatment. In order to specifically destroy cancer cells without harming healthy cells, therapeutic vaccines can be created to target cancer-specific antigens in the patient's body or particular proteins on the surface of cancer cells. In addition, therapeutic vaccines can also activate the immune system of patients, induce specific immune responses, and enhance the ability of immune system to recognize and attack tumors. The mechanism of therapeutic vaccines was also elaborated. The basic principle of therapeutic cancer vaccines is that some specific antigens, or epitopes, are specifically expressed in cancer cells, and these antigens can induce the immune system to activate immune cells. Showed the clinical efficacy of existing therapeutic vaccine products. The FDA has approved the sale of three therapeutic cancer vaccines. Meanwhile, many types of cancer vaccines are also undergoing clinical trials. In 2015, the T-VEC was approved for the TalimoginilahPa virus. This is the latest approved cancer vaccine. T-VEC is a vaccine targeting melanoma, based on the HSV, which also incorporates the GM-CSF gene and the infectious cell protein 2 gene. The effectiveness of T-VEC was confirmed in its final report in 2019, with significantly higher DRR and ORR in the treatment group compared to the control group. Recently, some trials of T-VEC treatment alone have shown good safety and other benefits. Although there is no approved therapeutic vaccine for breast cancer, there are still many breast cancer vaccines in clinical trials. NeuVax entered a phase 3 clinical trial (NCT01479244) but was terminated due to its low efficacy. In breast cancer tissues, HER2 has characteristic expression, so many breast cancer vaccines use HER2 as a target. Pointed out the current problems and technical challenges of therapeutic vaccines. Overall, therapeutic vaccines have advantages over traditional therapies in terms of specific treatment and stimulating the immune system to participate in treatment. However, further clinical research and validation are still needed to improve the efficacy and safety of treatment.

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