

Clinical Progress of Traditional Chinese Medicine in Treating Adverse Reactions after Breast Cancer Surgery and Chemotherapy

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Abstract: *Breast cancer is a malignant tumor with a high incidence rate. Its pathogenesis may be related to genetic, hormonal, reproductive, dietary, radiation, and drug factors. The main clinical manifestation is a painless breast lump. Modern medical treatments include surgery, radiotherapy, chemotherapy, endocrine therapy, and molecular targeted therapy. Although these treatment modalities can achieve considerable efficacy, their adverse reactions are also significant and seriously affect patients' physical and mental health. In traditional Chinese medicine (TCM), breast cancer falls under the category of "Breast Rock". Studies have found that TCM can effectively improve postoperative skin flap necrosis and upper limb lymphedema, alleviate chemotherapy-induced gastrointestinal reactions, improve chemotherapy-induced myelosuppression, and regulate endocrine disorders.*

Keywords: Breast cancer, Traditional Chinese medicine, Chemotherapy, Adverse reactions.

1. Introduction

On April 4, 2024, "CA: A Cancer Journal for Clinicians" published the "Global Cancer Statistics 2022" jointly compiled by the International Agency for Research on Cancer and the American Cancer Society. The report shows that breast cancer has a particularly severe impact on women's health globally, with the highest incidence among women, accounting for one-quarter of newly diagnosed cancer cases and one-sixth of cancer deaths in women worldwide [1]. Breast cancer has become a major public health issue globally, and the task of prevention and treatment remains arduous.

Breast cancer is a disease characterized by malignant transformation of epithelial cells in the mammary ducts and lobules under the influence of various carcinogenic factors, with a painless breast lump as the main clinical feature. Its etiology is complex and closely related to genetic factors, hormone levels, reproductive health, nutritional status, and environmental factors. Currently, treatment of breast cancer is typically based on surgery, supplemented by radiotherapy, chemotherapy, endocrine therapy, and molecular targeted therapy. Although Western medical treatment is the mainstay and achieves certain efficacy, its adverse reactions seriously affect patients' quality of life and treatment adherence. In recent years, TCM has been increasingly widely applied in alleviating and treating postoperative and post-chemotherapy adverse reactions. Chinese herbal medicine, with its multi-target effects and low toxicity, plays advantages in reversing drug resistance, inhibiting metastasis and recurrence, blocking the cell cycle, and promoting cell death of breast cancer cells. Moreover, it can holistically regulate the patient's physical condition, playing a crucial role in breast cancer treatment [2].

2. TCM for Alleviating or Treating Postoperative Complications of Breast Cancer

2.1 Postoperative Skin Flap Necrosis

Currently, surgical resection remains the mainstay of breast cancer treatment. Although clinical treatment plans are continuously improving, postoperative complications such as subcutaneous fluid accumulation and skin flap necrosis remain unavoidable [3]. Radical mastectomy usually requires removal of the entire breast, pectoralis major and minor muscles, and dissection of axillary and subclavian lymph nodes. This procedure involves extensive surgery, and due to extensive flap separation, the flap may become too thin or uneven in thickness during dissection, damaging capillaries in the dermis and affecting postoperative blood supply. Additionally, excessive tension during flap suturing or postoperative wound effusion can also induce ischemic necrosis of the flap. Western medical management of flap necrosis mainly involves excision of the necrotic flap and re-implantation of a new flap. TCM often uses external application therapy. Wang Fei [4] randomly divided 40 patients undergoing modified radical mastectomy into two groups: the control group received routine iodine disinfection, while the observation group received additional external application of Yuling Liquid. Results showed that the effective rate in the observation group was 100%, higher than 75% in the control group, indicating that Yuling Liquid can effectively reduce the occurrence of flap necrosis and promote flap recovery. Tong Yao et al. [5] randomly divided 40 breast cancer patients with postoperative local flap necrosis into a treatment group and a control group. The former received Huafu Shengji Ointment for dressing changes, while the latter received Mupirocin ointment. The shedding time of necrotic tissue and the appearance time of new epithelium were observed and recorded; both indicators in the treatment group were superior to those in the control group, demonstrating that Huafu Shengji Ointment has significant effects in promoting healing of refractory wounds caused by postoperative flap necrosis.

2.2 Upper Limb Lymphedema

After radical mastectomy, patients often develop upper limb edema due to obstructed lymphatic and blood return. Currently, Western medicine is commonly used to treat lymphedema in the affected limb. Furosemide, as a diuretic, can effectively promote excretion of water and electrolytes, thereby significantly alleviating edema. However, long-term use may cause various adverse reactions and even renal impairment, and its efficacy in severe edema is not ideal [6,7]. Su Ying selected 76 breast cancer patients with postoperative lymphedema; the control group was treated with furosemide, while the treatment group received modified Fangji Huangqi Decoction. Results showed that the total effective rate in the treatment group was significantly higher than that in the control group. After treatment, the difference in upper limb circumference between the affected and healthy sides in the treatment group was significantly smaller than that in the control group. Pain scores were also lower in the treatment group, while the incidence of adverse reactions was lower in the control group. Moreover, CD^{4+} cells, CD^{8+} cells, CD^{4+}/CD^{8+} ratio, and IL-17 levels in the treatment group were superior to those in the control group, suggesting that modified Fangji Huangqi Decoction can significantly improve pain and edema symptoms and reduce adverse reactions in patients with postoperative lymphedema. Liu Keqiao randomly divided 62 eligible patients into two groups: the control group received functional exercise, while the treatment group received functional exercise combined with wet compress of a self-formulated Huoxue Tongluo Xiaozhong Formula. Comparison of lymphedema severity showed an effective rate of 86.67% in the treatment group versus 63.33% in the control group, indicating that the combination can reduce limb circumference, alleviate discomfort, and improve quality of life. Zhang Lifang [8] randomly divided 98 patients with different degrees of postoperative edema into a control group (routine rehabilitation training) and a treatment group (routine training plus modified Chinese herbal hard plaster application). Results showed that the bilateral upper arm circumference difference in the treatment group was significantly lower, and upper limb lymphatic flow was significantly higher than in the control group, suggesting that modified Chinese herbal hard plaster combined with routine rehabilitation training is more effective in reducing lymphedema.

3. TCM Treatment of Post-Chemotherapy Adverse Reactions

3.1 Gastrointestinal Reactions

Chemotherapy plays a vital role in breast cancer treatment by effectively eliminating subclinical micrometastases in lymph nodes and distant organs. However, the toxic side effects of chemotherapeutic agents seriously affect patients' quality of life and weaken their confidence in treatment. The most common adverse reaction during chemotherapy is nausea and vomiting, which is also one of the most distressing side effects and often leads many patients to abandon chemotherapy [9]. Chemotherapeutic drugs primarily act by promoting the release of 5-hydroxytryptamine from enterochromaffin cells in the gastrointestinal mucosa, which stimulates 5-HT receptors in the central and peripheral nervous systems,

inducing nausea and vomiting [10]. According to TCM theory, breast cancer belongs to the syndrome type of "root deficiency and branch excess". Although the tumor mass is removed after surgery, residual toxins remain in the body, further damaging healthy qi. Therefore, treatment must address both strengthening the body's resistance and eliminating pathogenic factors, with strengthening resistance playing a particularly important role throughout the entire TCM treatment process [11]. Gao Yinyin [12] randomly divided 80 pediatric leukemia patients undergoing chemotherapy into a control group and an observation group. Both received routine chemotherapy, but the control group received only routine nursing, while the observation group received additional auricular point pressing therapy. Results showed that the frequency, severity, and duration of vomiting in the observation group were significantly lower than in the control group, indicating that auricular point pressing is significantly effective in alleviating nausea and vomiting in leukemia patients undergoing chemotherapy. Chen Ziyin [13] divided 74 female breast cancer patients receiving anthracycline - cyclophosphamide regimens into a control group (routine antiemetic treatment) and a treatment group (Lingnan fire-needle therapy combined with routine antiemetic treatment), with acupoints including Zusanli (ST36), Zhongwan (CV12), Neiguan (PC6), and Chize (LU5). Results showed that within 24 hours after chemotherapy, the complete remission rate and total control rate of vomiting in the treatment group were significantly higher than those in the control group, indicating that Lingnan fire-needle therapy combined with conventional antiemetics can effectively control acute vomiting, reduce nausea severity, and improve appetite.

3.2 Myelosuppression

Myelosuppression refers to damage to hematopoietic stem cells in the bone marrow, rendering them unable to effectively replenish peripheral blood cells, resulting in a decrease in all three cell lineages. Among them, white blood cells (WBC) have a relatively short half-life of only 6-8 hours; therefore, leukopenia is often the earliest manifestation in peripheral blood counts during chemotherapy-induced myelosuppression [14], followed by thrombocytopenia and eventually severe anemia. Commonly used Western drugs for post-chemotherapy myelosuppression include Leucogen, Vitamin B4, and Batyl alcohol. These conventional drugs have been used clinically for decades. Although the treatment course is long, they can still restore WBC levels to normal in patients with grade I and II leukopenia. However, for grade III and IV leukopenia, the effective rate is only about 40% [15]. Du Yue et al. [16] randomly divided 50 breast cancer patients with TCM pattern of liver-kidney yin deficiency and qi-blood insufficiency into two groups based on a random table and patients' willingness to take oral Chinese herbal decoctions long-term. The study group received Yisui Shengbai Formula starting from the first day of chemotherapy, while the control group received Yangzheng Heji, a Chinese patent medicine. Peripheral WBC and neutrophil (NE) counts were recorded on days 1, 7, and 14 after chemotherapy. Results showed no statistically significant difference in baseline WBC and NE values between groups. On day 7, the mean WBC in the study group was slightly higher than in the control group, and on day 14, it was significantly higher, indicating that Yisui

Shengbai Formula has a marked effect on elevating WBC and NE counts in breast cancer patients with post-chemotherapy myelosuppression. Xiong Luya [17] found that most breast cancer patients with post-chemotherapy myelosuppression present with spleen-kidney yang deficiency. Fuyang Fire Moxibustion could significantly improve myelosuppression in this pattern, increase peripheral WBC and NE counts, and alleviate spleen-kidney yang deficiency symptoms. Luo Yingzhe [18] observed the efficacy of Xiangsha Liujunzi Decoction in ameliorating post-chemotherapy myelosuppression and found that it could reduce the incidence and severity of NE and platelet (PLT) suppression and improve quality of life. Qiu Xiaowei [19] found that moxibustion at Qihai (CV6), Guanyuan (CV4), and Zusanli (ST36) could improve post-chemotherapy myelosuppression, promote recovery of bone marrow hematopoietic structure and function in tumor-bearing mice, and facilitate neutrophil maturation.

4. TCM for Alleviating Adverse Reactions of Endocrine Therapy

Studies have shown that breast cancer is one of the hormone-dependent tumors, and endocrine therapy may have good efficacy in controlling disease progression and alleviating clinical symptoms [20]. However, due to the long treatment course and abnormal hormone levels, endocrine therapy is accompanied by a series of adverse reactions, such as menopausal-like syndrome, lipid metabolism disorders, bone-related adverse events, endometrial thickening and other gynecological reactions, as well as decreased immunity and drug resistance after long-term treatment [21].

4.1 Menopausal-Like Syndrome

Under endocrine therapy, estrogen levels decrease, leading to imbalance of endocrine regulation in sex hormone target organs and dysfunction of the hypothalamic-pituitary-gonadal axis, manifesting as hot flashes, night sweats, depression, irritability, insomnia, and alternating chills and fever. Clinically, these symptoms resemble those seen in perimenopausal women and are termed menopausal-like syndrome. According to symptom presentation, it can be classified into categories such as “depression syndrome” and “visceral agitation”. Xiong Changzhou [22], based on the “heart-liver correlation” theory, applied Xiaoyao San combined with Ganmai Dazao Decoction to treat breast cancer-related depression. The study found that this combination effectively improved depressive symptoms, with efficacy superior to Flupentixol-Melitracen tablets and no obvious toxic side effects.

4.2 Osteoporosis

For HR-positive patients, third-generation aromatase inhibitors (AIs), represented by letrozole, are first-line endocrine therapy agents. AIs inhibit or inactivate aromatase in the adrenal glands, liver, and adipose tissue, thereby reducing estrogen levels [23]. Estrogen reduction leads to bone metabolic imbalance, with increased bone resorption and decreased bone formation, resulting in trabecular bone rarefaction and accelerated bone loss, causing reduced bone calcium and secondary osteoporosis, increasing fracture risk.

TCM holds that breast cancer endocrine therapy-related osteoporosis involves multiple organs and viscera, with kidney deficiency as the main cause, spleen deficiency as an important cause, liver depression as a key factor, and blood stasis as a promoting factor [24]. Chen Juan et al. [25] randomly divided 100 breast cancer patients with endocrine therapy-induced osteoporosis into a study group and a control group. The study group received Qing'e Pills combined with calcium supplements, while the control group received calcium alone. Bone mineral density (BMD) was measured at 6 and 12 months after treatment. Results showed that BMD in the study group was significantly higher than in the control group at both time points, indicating that Qing'e Pills combined with calcium significantly improves BMD in these patients.

4.3 Endometrial Lesions

Selective estrogen receptor modulators (SERMs), represented by tamoxifen and toremifene, are commonly used endocrine therapy drugs. While inhibiting ER-positive breast cancer cell growth, they also stimulate endometrial cell proliferation, leading to endometrial thickening, polyps, inflammation, and even malignancy. Xia Tingting [26] randomly divided 60 ER-positive breast cancer patients into two groups: the treatment group received modified Guizhi Fuling Pills combined with tamoxifen, while the control group received tamoxifen alone. Endometrial thickness was compared before and after one treatment cycle (12 weeks). Results showed a significant difference in endometrial thickness before and after treatment in the treatment group, but no significant difference in the control group, indicating that modified Guizhi Fuling Pills reduce the incidence of SERMs-induced endometrial hyperplasia in ER-positive breast cancer patients receiving endocrine therapy.

5. Summary and Prospects

The incidence of breast cancer in China remains high. Although conventional therapies such as surgery, radiotherapy, chemotherapy, and endocrine therapy can achieve certain efficacy, their adverse reactions require attention, as they may lead to treatment interruption and loss of anticancer confidence. Nowadays, TCM plays an increasingly prominent role in breast cancer treatment, applying holistic concepts and syndrome differentiation to alleviate post-chemotherapy and endocrine therapy adverse reactions. However, there are still certain shortcomings, such as insufficient sample sizes. With the advancement of modern medicine and clinical research on breast cancer, breakthroughs are expected in the use of TCM to alleviate postoperative and post-chemotherapy adverse reactions.

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