Literature Study

Clinical progress on moxibustion in preventing and treating adverse effects of surgery or chemoradiotherapy for breast cancer

艾灸防治乳腺癌手术及放化疗不良反应的临床研究进展

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Abstract

Breast cancer has the highest incidence rate among all women's malignant tumors worldwide. Surgery, radiotherapy and chemotherapy are three major treatments, while most patients showed adverse effects or complications during or after the treatment, including lymphedema, gastrointestinal reactions and leukopenia, which cause severe impact on patients' recovery and quality of life. Moxibustion has been used and certified to alleviate adverse effects of surgery or chemoradiotherapy for breast cancer. We have summarized literatures in recent years and suggest more systematic research in the future for the underlying mechanism.

Keywords: Moxibustion Therapy; Acupuncture-moxibustion Therapy; Breast Neoplasms; Postoperative Complications; Chemoradiotherapy; Lymphedema; Women; Review

【摘要】乳腺癌是全球女性发病率最高的恶性肿瘤。手术、放射治疗和化疗是当前治疗乳腺癌的三大手段,但多数患者在治疗当中或之后易出现不良反应和并发症,如淋巴水肿、胃肠道反应、白细胞减少症等,严重影响乳腺 癌患者的手术及放化疗后的恢复和生活质量。艾灸防治乳腺癌手术及放化疗的不良反应已在临床上有所实践,疗 效肯定。本文就近年来有关文献进行总结,建议今后的研究中进一步加强系统化研究以明确作用机制。

【关键词】灸法; 针灸疗法; 乳腺癌; 术后并发症; 放化疗; 淋巴水肿; 女性; 综述

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Breast cancer (BC) has the highest incidence rate among all women's malignant tumors worldwide. Statistics show that the incidence of BC has been significantly rising in recent years in Asia where used to have a low incidence^[1]. Surgery, radiotherapy and chemotherapy are three major treatments while most patients show adverse effects or complications during or after the treatment^[2]. Traditional Chinese medicine (TCM) has shown advantages in treating the adverse effects or complications of surgery or chemoradiotherapy^[3]. Moxibustion is a common external treatment approach in TCM. It functions to warm meridians, move qi and activate blood, resolve dampness and cold and disperse nodules. It can also adjust human organisms

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and promote immune functions. As a non-invasive treatment, moxibustion is convenient, effective and cheap. In addition, it helps to alleviate adverse effects of surgery or chemoradiotherapy. We have made a brief analysis of the clinical status of moxibustion in treating adverse effects of surgery or chemoradiotherapy for BC.

1 Post-surgery Lymphedema

1.1 Overview of TCM and Western medicine research

Post-surgery upper limb lymphedema is a common complication in BC patients and the incidence rate may approach 65%. Interventions including axillary lymph node dissection, chemotherapy and radiotherapy will all lead to lymphedema of the affected limb^[4]. The main causes are obstructed lymphatic circulation caused by surgery; moreover, obstructed venous return caused by wound or pressure during binding will all add up to lymphedema^[5].

TCM holds that edema is caused by blocked blood circulation. BC and surgery can obstruct meridians, cause gi stagnation and blood stasis, and then water flow is blocked and dampness accumulates into edema^[6]. Besides, BC is characterized by deficiency in root and excess in symptoms, and patients are short of healthy yang qi, adding the consumption of qi and blood during surgery, so that body is too weak to circulate water and finally edema occurs. Sun L, et al^[7] found that blood stasis was the pathological basis for upper limb edema after BC surgery, in turn, complications including flap necrosis, subcutaneous effusion and swelling of the affected limbs would aggravate blood stasis. Moxibustion combined with special acupoints has obvious advantages over moving qi and water, activating blood and removing stasis.

1.2 Overview of moxibustion for limb lymphedema after BC surgery

1.2.1 Single moxibustion therapy

Modern research has shown that moxibustion can warm yang to disperse dampness and cold, unblock meridian to alleviate edema. It is effective in improving deficiency, cold and stasis. First, by functioning on surface, its medicinal substance can enter into body by inhalation or diffusion to calm the mind. Then, the light and heat radiation generated by moxibustion can promote local blood and lymph circulation, eliminate inflammation and edema, and facilitate immune function to increase the activity of macrophagocytes, alleviate proliferation of cicatricial tissue and edema. Thus single moxibustion has a therapeutic effect for post-surgery lymphedema.

Liu Y^[8] randomized 100 BC patients into two groups. All patients received modified radical mastectomy and chemoradiotherapy. Fifty patients in the treatment group received routine nursing care plus suspended mild moxibustion applied along the Pericardium Meridian on the affected limb, from Laogong (PC 8) to Tianguan (PC 2), 5 min for each point, once a day, 5 d in a week. Patients in the control group received routine nursing care alone. After 2 months, the upper-limb lymphedema status was compared. The result showed that the incidence of lymphedema in the treatment group was substantially lower than that in the control group, showing a statistical significance (P<0.05). The size of edema was smaller in the treatment group (P<0.05). Therefore, moxibustion can obviously reduce the incidence and size of upper-limb lymphedema after BC surgerv.

Li SM, *et al*^[9] observed 80 BC patients who had received modified radical mastectomy and periodical chemotherapy. Forty patients were selected to receive mild moxibustion at acupoints of the Pericardium Meridian, including Tianquan (PC 2), Quze (PC 3), Neiguan (PC 6), Daling (PC 7) and Laogong (PC 8), 3 d as

a course, for 3 courses on the basis of routine nursing care. Patients in the control group only received routine nursing care. The incidence and degree of limb edema were compared before and after the treatment. Between-group comparison showed that patients in the treatment group had a lower incidence and degree of edema than those in the control group (P<0.05), along with a better quality of life (QOL) score, physiological, emotional and functional status, and the betweengroup comparisons showed statistical significances (P<0.05). Intra-group comparison showed an alleviation of edema in the treatment group (P<0.05), while no statistical significance showed in the control group before and after the treatment (P>0.05). The QOL and functional score in the treatment group was higher than that before the treatment (P<0.05), and the scores of QOL, physiological, and emotional status dropped in the control group after the treatment (P<0.05). Therefore, moxibustion was considered effective in preventing limb edema in patients after BC surgery and undergoing chemotherapy, and also in improving patients' QOL.

Lou XJ, et al^[10] observed 130 patients of post-surgery BC and randomized them into a treatment group of 65 cases and a control group of 65 cases. Patients in the treatment group received breast function rehabilitation exercise combined with moxibustion. The acupoints included Danzhong (CV 17), Jianzhongshu (SI 15), Tianzong (SI 11), Zusanli (ST 36), Guangming (GB 37) and Yinlingquan (SP 9). Prevention methods were used for patients who had not showed edema, and treatment methods for those who had showed. Moxibustion and routine functional rehabilitation were applied since 5 d after the surgery (removed the chest belt), once a day, 30 min each time. For prevention, one course lasted for 15 d, and 1 month for treatment. The result showed that compared with routine functional rehabilitation, moxibustion plus routine functional rehabilitation had a better therapeutic effect (P<0.05).

1.2.2 Moxibustion plus tuina manipulation

Tuina manipulation like Rou-kneading along meridians can increase the exercise load of limbs, relax local muscle tissue, relief muscle numbness, prevent muscle atrophy and also promote local venous and lymph circulation. Combined with moxibustion, it can substantially relieve post-surgery edema.

Liu YH^[11] observed 80 BC patients who had received modified radical mastectomy by randomizing them into 2 groups. Forty patients in the treatment group received moxibustion at acupoints plus tuina therapy. The manipulation started 1 d before chemotherapy, together with mild moxibustion at Tianquan (PC 2), Quze (PC 3) and Neiguan (PC 6) from the Pericardium Meridian on the affected limb. The treatment was conducted every morning, 4 d as a course, for 3 courses. Patients in the control group received routine nursing care. Then the edema status was compared. The result showed that the incidence of edema in the treatment group was lower than that of the control group (P<0.05), the diameters of elbow and upper limbs were lower than those in the control group (P<0.05). Therefore, it's concluded that moxibustion plus acupoint tuina therapy can prevent upper-limb edema in post-surgery BC patients.

Wang TS, *et al*^[12] applied the therapy of Roukneading to acupoints including Tianquan (PC 2), Quze (PC 3), Daling (PC 7), Laogong (PC 8) and Zhongchong (PC 9) on the basis of routine limb rehabilitation exercise for 30 patients, once a day for 15 successive days, while the limb rehabilitation exercise alone for other 30 patients. The functional texts were done respectively 20 d and 30 d after modified radical mastectomy surgery. The result showed that the therapeutic effect in the treatment group was superior than that in the control group (*P*<0.05).

1.2.3 Moxibustion plus acupuncture

Moxibustion plus acupuncture has the function of reinforcing the healthy qi and eliminating the pathogenic factors, regulating yin and yang and warming meridians. Specific acupoints have the function of warming yang to help circulate blood and water flow, and consequently relieve upper limb edema.

Chen JJ, et al^[13] recruited 30 BC patients with chronic lymphedema, and randomized them into a treatment group and a control group, 15 cases in each group. The treatment group received acupuncture and moxibustion every other day, and the points were selected by local point-selection principle as basis, accompanied by pattern differentiation principle for distal points, including Jianyu (LI 15), Waiguan (TE 5), Quchi (LI 11), Shuifen (CV 9), Yinlingquan (SP 9) and Zusanli (ST 36). Even reinforcing-reducing manipulation was applied during acupuncture. The needles were retained for 30 min after manipulation. During needle retaining, moxa stick of 3 cm in length was used to apply suspended moxibustion to each point. One treatment lasted for 30 min, 28 d as a course. Patients in the control group received oral administration of diosmin everyday. The diameter of upper limb and shoulder joint mobility were measured before the treatment and after 7, 14, 21 and 28 d of treatment, as well as QOL. The result showed that acupuncture and moxibustion can obviously improve post-surgery edema degree, produce equivalent effect in improving shoulder joint mobility compared with diosmin, and thus is an effective and safe method to alleviate edema, improve shoulder mobility and increase QOL.

1.2.4 Moxibustion plus external treatment method of Chinese medicine

Medicine with function of activating blood and

resolving stasis can penetrate skin and be absorbed by mucous membrane to improve microcirculation and increase vascular permeability, so that it can activate blood, remove stasis and alleviate edema^[14]. External treatment of Chinese medicine plus moxibustion can facilitate the clearance and absorption of stasis and fluid, so as to accelerate the recovery of edema.

Zeng YD^[14] found that on the basis of upper-limb functional rehabilitation and intravenous drip of *Dan Shen* (*Radix Salviae Miltiorrhizae*) injection to treat post-surgery BC patients, adding external rinsing with medicinal decoction including *Su Mu* (*Ligum Sappan*), *Shen Jin Cao* (*Herba Lycopodii*) and *Chi Shao* (*Radix Paeoniae Rubra*), plus moxibustion at acupoints including Tianquan (PC 2), Guanyuan (CV 4), Neiguan (PC 6), Zusanli (ST 36) and Quze (PC 3) can generate a better therapeutic effect for upper-limb edema.

He NY^{[15]'} treated 60 BC patients. The treatment group was treated by external application of Chinese medicine plus electronic moxibustion and thermal therapy. The medicinal powders including Huang Qi (Radix Astragali), Gui Zhi (Ramulus Cinnamomi) and Ji *Xue Teng (Caulis Spatholobi)* were mediated with honey and pasted on local skin with edema. The paste was changed every day. Moxibustion was used for acupoints including Guanyuan (CV 4), Shuifen (CV 9), Hegu (LI 4), Neiguan (PC 6), Waiguan (TE 5), Quze (PC 3), Binao (LI 14) and Jianjing (GB 21). Patients in the control group were treated with intravenous drip of glucose plus Dan Shen (Radix Salviae Miltiorrhizae) injection in combination with upper-limb functional rehabilitation exercise. The result showed that the effective rate in the treatment group was superior to that in the control group (P<0.05) and proved the effectiveness of such treatment approach.

2 Gastrointestinal Reactions Caused by Chemotherapy

2.1 Overview of TCM and Western medicine research

Gastrointestinal reactions are common among most cancer patients undergoing chemoradiotherapy. Common symptoms include diarrhea, mucositis and vomiting. Medicine of chemotherapy may alter intestinal flora, and activate 5-hydroxytryptamine (5-HT) receptor in central and vagus nerves, thus generate severe gastrointestinal reactions. Besides, patients receiving chemotherapy are easily getting nervous and tense, leading to gastrointestinal reactions. All these reactions will undermine patients' compliance, and lead to the reduction or even intermittence of the treatment.

TCM holds that cancer is a root-deficient and manifestation-excess pattern with insufficient yang qi. Treatment like surgery and chemotherapy will lead to weakness of spleen and stomach, devitalization of spleen yang, retained water, and reverse flow of stomach qi, consequently causing gastrointestinal diseases. Emotional factor is also a pathogenic factor. Moxibustion at specific acupoints like Shenque (CV 8), Zhongwan (CV 12) and Zusanli (ST 36) has the function of warming spleen to disperse cold, harmonizing the stomach to cease vomiting, settling fright and tranquilizing. Therefore, it can alleviate gastrointestinal reactions.

Other research showed that environment, metabolism, infection and genetics factors can influence the opening of Toll-like receptors (TLRs) pathway, which can innate immunity to affect gastrointestinal toxicity of chemotherapy. Further research should start from immunity to restrain the toxicity of chemotherapy^[16]. Therefore, moxibustion is speculated to alleviate gastrointestinal reactions by benign regulation of the immunity.

2.2 Overview of moxibustion for the treatment of gastrointestinal reaction following chemotherapy in BC patients

Ye YQ, et al^[17] selected 98 BC patients receiving CE(T)F chemotherapy and randomized them into two groups. The ginger-partitioned moxibustion group received moxibustion at Shengue (CV 8), Zhongwan (CV 12), Neiguan (PC 6) and bilateral Tianshu (ST 25), Daheng (SP 15) before and after chemotherapy, while the control group received intravenous injection of 5-hydroxytryptamine receptor type 3 (5- HT_3) once for blocker before chemotherapy. After 3 d, gastrointestinal reactions in both groups were observed. The results showed that the therapeutic effect of the gingerpartitioned moxibustion group in preventing and treating nausea and vomiting in BC patients were superior to that of the control group. No adverse events showed during the treatment, indicating the safety of such treatment.

Hu CJ, *et al*^[18] treated chemotherapy-induced gastrointestinal reactions with moxibustion at Zhongwan (CV 12), Shenque (CV 8) and bilateral Zusanli (ST 36) for 10 min plus self-made vomit-stopping paste on the basis of routine western medicine treatment, and compared it with routine Western medicine treatment alone. The results showed that patients in the treatment group had lower vomiting, nausea and constipation rate and severity during and after chemotherapy (*P*<0.05). Thus this approach was considered effective in preventing gastrointestinal reactions and easy to conduct.

Zhong SW, *et al*^[19] selected 58 patients who met the inclusion criteria, and divided them into a treatment group and a control group. Both groups received intravenous injection of granisetron hydrochloride once before and after chemotherapy for vomit-stopping treatment. Patients in the treatment group received

ginger-partitioned moxibustion at acupoints including Shenque (CV 8), Zhongwan (CV 12), bilateral Neiguan (PC 6) and Zusanli (ST 36), 10 min for each point, starting 1 d before chemotherapy, once a day for 3 d. Gastrointestinal reactions from 1-7 d of chemotherapy were observed. The result showed that the extension of vomiting and nausea from day 2-7 between the two groups showed significant differences, indicating a better effect in the treatment group, and showing that moxibustion can effectively improve nausea and vomiting following chemotherapy for BC, and improve QOL.

Fang X, *et al*^[20] found that on the basis of intravenous injection of vomit-stopping medicine, carry-on moxibustion (warm moxibustion box) at Zhongwan (CV 12) plus acupoints massage could effectively alleviate vomiting following chemotherapy. Such method can harmonize spleen and stomach, stop vomiting and regulate qi to soothe the chest to alleviate sufferings of the patients.

3 Leukopenia After Chemotherapy for BC

3.1 Overview of TCM and Western medicine research

Chemotherapy is an essential treatment for BC patients. However, while killing cancer cells, it also harms healthy cells and immune function, and reduces leukocytes. At present, traditional methods including oral administration of batyl alcohol and vitamin B₄ can increase leukocyte while with a high cost and limited effect^[21]. Modern research showed that moxibustion has the function of warming meridian and activating blood. It can build up constitution, boost immune capability, improve the activity of serum granulocytemacrophage colony stimulating factor (GM-CSF), reduce injury to hematopoietic stem cell, alleviate bone marrow inhibition caused by chemotherapy and increase leukocyte count^[22]. It's also a convenient, lowcost and effective approach for leukopenia after chemotherapy, though the mechanism requires further investigation.

3.2 Overview of moxibustion treatment for leukopenia after chemotherapy in BC patients

Wu HQ, *et al*^[23] used herb-partitioned moxibustion at umbilicus to facilitate chemotherapy for BC and observed the clinical effect. The herbal prescription was composed of Sheng Mai Yin (Pulse-activating Decoction) and Dang Gui Bu Xue Tang (Angelicae Sinensis Decoction for Supplementing Blood). The total effective rate was 84.0%, indicating that such method can control leukopenia after chemotherapy and improve immune function.

Yue SB, et $al^{[24]}$ selected 60 BC patients under chemotherapy with leucopenia. They were divided into an observation group and a control group, 30 cases in

each group. Patients in the observation group received tapping the Bladder Meridian on the back and ginger-partitioned moxibustion on the Governor Vessel. The control group received recombinant human granulocyte colony-stimulating factor (rhG-CSF) and/or batyl alcohol pills. The change in leukocyte count was measured before and after the treatment. The result showed that the therapeutic effect in the treatment group was better than that in the control group, showing a statistical significance (P<0.05). It's indicated that the method is effective for leukopenia.

Cheng L, *et al*^[25] randomized 102 cancer patients taking chemotherapy into a treatment group of 52 cases (including 11 cases of BC) and a control group of 50 cases (including 10 cases of BC). With medical intervention to make sure the leukocyte count was above 4.0×10^9 /L, the treatment group received moxibustion at Zusanli (ST 36), once a day, 15 min each treatment. While, the control group orally took leucogen pills. After 3 weeks, the total effective rate between the two groups showed a significant difference (*P*<0.05), indicating that moxibustion treatment can reduce the inhibition of chemotherapy drugs on bone marrow and increase leukocyte count.

4 Limb Movement Disorder After BC Surgery

4.1 Overview of TCM and Western medicine research

Limb movement disorder is a common adverse reaction in BC surgery, manifested as shoulder joint movement limitation, muscle atrophy, partial sensory disturbance and weakness which will gravely impact QOL and rehabilitation process, as well as bad emotions. Three main causes for limb movement disorder are edema due to poor lymphatic drainage, cicatrix due to large cuts during surgery, and pain^[26]. TCM holds that BC surgery may injure qi and blood and break meridians, and the subsequent improper gi-blood movement and malnutrition of sinew can lead to movement dysfunction. So, the treatment should focus on activating blood, moving qi and warming meridians. Moxibustion on joints or along meridian can dredge meridians and improve gi-blood movement, and also regulate body function, nourish skin, soften scar, improve immunity and finally improve limb movement. 4.2 Overview of moxibustion on limb movement disorder in post-surgery BC patient

Sun L, *et al*^[27] treated patients with moxibustion at Jianjing (GB 21), Jianliao (TE 14), Jianzhen (SI 9), Binao (LI 14) and Ashi points on the affected side based on routine functional rehabilitation, and compared such treatment with functional exercise alone. The upper-limb grip force was tested. The result showed that the functional recovery of shoulder joint in the treatment group was superior to that in the control group (P<0.05).

In the treatment group, 15 d after the surgery, the strength showed no statistical difference when compared with that before the surgery (*P*>0.05), showing an obvious recovery of grip force. Thus, moxibustion was proven effective in improving functional disorder of the affected limb in post-surgery BC patients, and also in accelerating the rehabilitation process.

Wang HJ, *et al*^[28] divided 60 patients into two groups. Patients in the control group received individualized progressive functional exercise, while those in the treatment group received moxibustion at Jianqian (Extra), Jianyu (LI 15), Jianzhen (SI 9), Quchi (LI 11), Waiguan (TE 5) and Hegu (LI 4), 10 min for each point, twice a day, followed by the same functional exercise done 10 min after moxibustion. The result showed that joint mobility and muscle strength were all superior in treatment group (P<0.05), and thus held that traditional moxibustion treatment plus functional rehabilitation exercise can promote recovery of post-surgery limb functions, decrease post-surgery disability and improve QOL.

Chen XJ, et al^[26] selected 70 patients who met the inclusion criteria and divided them into two groups. Thirty-five cases in the treatment group received routine nursing care plus shoulder joint local-controlled mild moxibustion [fixed the moxibustion bag around the affected shoulder joint, covering the area up to Jianjing (GB 21), down to Binao (LI 14), forward to Zhongfu (LU 1), and backward to Tianzong (SI 11) and Jianzhen (SI 9)], once a day, 30 min each time, for 7 d. The result showed that compared with the control group using routine treatment, the treatment group showed better shoulder movement degree (P<0.05), while the occurrence and severity of shoulder movement disability were all lower in the treatment group (P<0.05). Thus this treatment was considered effective in improving shoulder function disability in post-surgery BC patients.

5 Moxibustion for Wound Healing After BC Surgery

The wound in BC surgery is relatively large. Complications like subcutaneous effusion and infection are common, and will slow the healing process and affect rehabilitation. Modern research showed that moxibustion has anti-inflammation and antibiosis function. It can regulate immune system, improve microcirculation, boost the phagocytosis of white blood cells, promote the regeneration of granulation tissue and accelerate wound healing^[29].

Zhu YN, *et al*^[30] observed the function of moxibustion on wound healing in post-surgery BC patients, during which 30 patients received moxibustion at Dazhui (GV 14) and Sanyinjiao (SP 6), 15-30 min for each point, with supplementation skills. The result showed that healing time in the moxibustion group was substantially shorter than that in the routine nursing care group (P<0.05).

6 Summary

Above all, moxibustion can improve immune function in post-surgery BC patients or those during chemoradiotherapy. It can move qi and drain water, activate blood and remove stasis, and improve microcirculation. The effect of such treatment for adverse events following surgery or chemoradiotherapy is also a manifestation of the regulation function on human body. Moxibustion is an effective and safe method for adverse events following surgery or chemoradiotherapy, with great advantages and a prosperous future.

Besides, adverse events of surgery or chemoradiotherapy are common, including insufficient healthy gi, gi stagnation and blood stasis, blocked water movement and malfunction of immune system. So, moxibustion may be effective for many other cancerous diseases, like gastrointestinal reactions following surgery or chemoradiotherapy for malignant tumor, bone marrow inhibition, lymphedema, wound infection and emotional disturbance. Nevertheless, literature is still limited by now and such method still requires further investigation.

There are some limitations in clinical practice and studies of moxibustion for adverse reactions of surgery or chemoradiotherapy. First, the mechanism of this method is still in exploratory stage and requires further systematic research. Second, improper sterilization or patients' constitution may induce infection of the wound. Clinically, moxibustion manipulation is mainly depended on personal experience of practitioners but lacks systematic training. Therefore, further improvement of standardization is required. Finally, present research of moxibustion treatment for BC-related disorders is mainly focused on remediation of the adverse events following surgery or chemoradiotherapy. However, injuries during surgery are still inevitable. So, later research may consider the direct therapeutic function of moxibustion for BC and other cancerous diseases. In future clinical study, we need a further combination of modern medical approach, and conduct in-depth study to provide new thoughts for moxibustion treatment of adverse events following surgery or chemoradiotherapy for BC or other cancerous diseases.

Conflict of Interest

The authors declared that there was no potential conflict of interest in this article.

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