

Research Progress of Chinese Medicine in Treating Side Effects of Radiation Therapy for Lung Cancer

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Abstract: Radiation side effects, such as radiation pneumonia, bone marrow suppression, radiation skin injury, radiation esophagitis, etc., have a significant negative impact on patients' quality of life, radiation therapy effectiveness, and prognosis. Radiation therapy plays a significant role in the treatment of lung cancer. The majority of modern medical care is symptomatic, susceptible to infection and immunosuppression, etc. Chinese medicine offers several distinctive benefits. In order to offer treatment suggestions for clinical treatment and lessen the side effects of radiation therapy, this paper primarily covers the treatment of radiation therapy side effects for lung cancer from Chinese medicine and summarizes the clinical experience of various schools.

One of the cancerous tumors that poses a major threat to human health and life is lung cancer, which is being treated using various techniques such as surgery, chemotherapy, radiotherapy, targeted therapy, and immunotherapy; Radiotherapy is one of them, and as of now, the NCCN guidelines have made it clear that 3-dimensional conformal radiation treatment (3DCRT) is the minimal technical standard for the administration of radiotherapy in patients with locally advanced disease[1]. Despite ongoing technological breakthroughs, radiation therapy will unavoidably result in unfavorable side effects like radiation pneumonia, bone marrow suppression, and radiation esophagitis in addition to harming nearby cells and organs. Utilizing Chinese medicine to alleviate these negative effects has proven to have definite advantages. This study focuses on the negative effects caused by Chinese medicine in the treatment of lung cancer after radiotherapy in order to provide specific treatment recommendations for clinical practice.

1. Radiation Pneumonia

Radiation therapy can produce lung inflammation called radiation induced pneumonitis (RP)[2], which is the first sign of radiation-related lung damage. The most common clinical signs and symptoms of radiation pneumonitis include fever, coughing up sputum, shortness of breath, chest pain, and tightness. If radiation pneumonitis is not promptly and successfully treated, it may progress to radiation pulmonary fibrosis, which can be life-threatening in severe cases [3].The main

treatments used in Western medicine for radiation pneumonia include glucocorticoids, antibiotics, etc., but these medications have serious side effects, such as secondary infections, disorders of the bacterial flora, endocrine disorders, and inhibition of immune function. According to Chinese medicine, radiological pneumonia falls under the categories of "cough," "asthma," and "lung atrophy." Radiation is a hot, deadly evil that burns the lung ligaments, drains Qi and Yin, and eventually disrespects the lung ligaments, leading them to stagnate and develop sickness.

The trend of radiation pneumonia symptoms, therapy, and medication in Chinese medicine over the previous ten years was examined by Lin Yuejie et al [4]. The study's findings showed that the main TCM symptoms of radiation pneumonia were lung Yin deficiency, lung solid heat (heat toxicity), lung blood stasis, and lung Qi deficiency. The main treatments for radiation pneumonia included moistening the lung, nourishing Yin, clearing heat, benefiting Qi, energizing blood, and detoxifying the toxicity. Single herbal remedies like Radix Ophiopogonis, honey-fried licorice root, and Radix Glehniae were the most. Yao Yilin et al [5] selected 60 postoperative patients with stage IIIa non-small cell lung cancer, 30 patients in the control group were given postoperative conventional radiotherapy, and in the treatment group, postoperative conventional radiotherapy was supplemented with the formula of benefitting Qi and nourishing Yin (Astragalus membranaceus, Radix Glehniae, Asparagus, Coicis seed, almond, Cornus officinalis, Moutan peel, reed root, Houttuynia cordata, Trichosanthis fructus bark, Scutellaria baicalensis, Mulberry white peel), and when the incidence of radiation pneumonia was compared between the groups 2 months after radiotherapy, the treatment group's incidence (37.93%) was considerably greater. In contrast to the control group (85.19%), the incidence of radiation pneumonia was much lower, and the level of inflammation was noticeably less severe. 92 patients with acute radiation pneumonia following radiotherapy for lung cancer were chosen by Wan Xingfu et al. [6]; the treatment group received Sha Shen Mai Dong Tang (Radix Glehniae, Radix Ophiopogonis, polygonatum odoratum, radices trichosanthis, mulberry leaves, Houttuynia cordata, bitter almond, radix platycodi, Peony skin, raw Rehmannia, Chuanxiong, raw licorice) while the control group received methylprednisolone intravenously. The outcomes demonstrated that acute radiation pneumonia could be efficiently treated by combining Sha Shen Mai Dong Tang with reduction. Hu et al. [7] chose 126 patients who had radiation pneumonia of grades I to IV as a result of chest cancer treatment. Western medicine was used to treat the control group, whereas acupuncture was used to treat the observation group's lung diarrhea, spleen tonification, and renal benefit (selected points: Tiantu, Jiaohou, Dazhui, Fengmen, Lique, Fengchi, Quchi, Zhongfu, Zhongwan, Zusanli, Tianshu, Qihai, Danzhong, Sanyinjiao, Shenshu, Guanyuan). The outcomes shown that the combination of the reducing lung, tonifying spleen and tonifying kidney acupuncture methods with western medicine might treat radiation pneumonia by reducing the level of inflammatory response in the patient's body and enhancing lung function. Both Hou Wei et al. [8] and Yu Xinjiang et al. [9] investigated the efficacy and safety of compound Kushen injection for the prevention and treatment of radiation pneumonia in primary lung cancer. The findings from both studies indicated that compound Kushen injection could decrease the occurrence of radiation pneumonia with no overtly harmful side effects being noted.

2. Radiation Therapy-Induced Suppression of the Bone Marrow

Leukopenia, anemia, and thrombocytopenia are signs of bone marrow suppression, which might suspend treatment, reduce the effectiveness of therapy, or even result in serious infection and life-threatening circumstances. Component blood transfusion, the use of various blood cell colony-stimulating agents, hematopoietic stem cell transplantation, etc. are the mainstays of modern medical treatment. As the number of radiation treatments rises, these techniques' efficacy will

gradually decline, and problems such as allergy, dermatitis, and fever may appear [10]. The majority of academics categorize it as "deficiency of blood" or "deficiency of labor." Radiation, in the opinion of Professor Diao Benshu, is a heat-poisonous evil that not only depletes Qi, harms Yin and blood, but also readily impairs the operation of the spleen, kidney, and other organs, resulting in According to the theory of nourishing Qi and blood, strengthening the spleen and kidney, and preventing and treating from Qi and blood, spleen and kidney, the therapy should be based [11].

Yuan Liuqun [12] chose 60 cases of radiation therapy-related adverse reactions for non-small cell lung cancer with deficiencies of both Qi and Yin. The control group received one cycle of radiation therapy, and the treatment group received nourishing Yin and clearing formula (American ginseng, Astragalus membranaceus, Atractylodes, Poria Cocos, Ganoderma lucidum, Radix ophiorrhiza, adenophora tetraphylla, Scutellaria baicalensis, Oldenlandia diffusa, Paeony, Licorice) during radiation therapy, and the findings demonstrated that the formula's ability to nourish and clear the body could lessen radiation therapy's bone marrow suppression. Yuan Dong [13] divided 60 cases of lung cancer patients receiving radiation therapy into two groups: the control group and the Chinese medicine group. In the Chinese medicine group, patients received radiation therapy along with Chinese medicine (Composition of the lung-nourishing formula in Chinese medicine: 30g of Astragalus membranaceus, 15g of dendrobe, 10g of yam, 5g of rhizoma bletillae, 15g of Oldenlandia diffusa, and 10g of pericarpium citri reticulatae). When comparing the negative effects of the herbal group with the control group, the study's findings revealed that the rate of leukocyte and hemoglobin reduction in the herbal group was substantially lower ($P < 0.05$).

According to Huang Wenzhi et al. [14], the application of ShengXueBaoHeJi and Diyu Shengbai Tablets together had a superior effect on delaying leukocyte decline and lowering the severity of bone marrow suppression during radiation therapy. Tan Feng et al. [15] came to the conclusion that the primary cause of bone marrow suppression brought on by radiotherapy is "toxicity," which results in a lack of both Qi and blood, and that the primary goals of treatment should be to benefit the essence and fill the marrow, tonify the kidney. Ginseng Guben Oral can strengthen the essence while nourishing Yin and Qi. It is made from Ginseng Guben Pill and Liu Wei Di Huang Pill. The main drugs in the formula include ginseng, raw Rehmannia rehmannia, cooked Rehmannia rehmannia, cornus officinalis, yam, Radix Ophiopogonis, all of which promote bone marrow suppression. In the combination group and the basic radiation group, the incidence of bone marrow suppression was 30% and 69.4%, respectively, with a P value of 0.05 for each group. According to the study's findings, radiation for non-small cell lung cancer patients may cause less bone marrow suppression if they receive a compound Kushen injection [16]. Shao Yanyan et al. [17] chose 40 cases of patients with malignant tumors and divided them into treatment and control groups, adding Shenmai injection to the control group. The outcomes demonstrated that Shenmai injection might successfully lessen the bone marrow suppression brought on by middle and late phases of radiation. The main ingredients of Shenmai injection are ginsenosides and maitake saponins, which can protect the hematopoietic system. It is a herbal injection made from the Chinese herbal medicine red ginseng and maitake, which has the effect of nourishing the Yin, benefiting the Qi, and nourishing veins [18].

3. Skin Damage Brought on by Radiation Therapy

Early signs of radiation skin damage include localized itchiness and pain, and in more severe cases, peeling ulcers and localized infection or even bacteremia. Later signs include skin thinning and the creation of contracture scars. The primary forms of treatment used in Western medicine are topical medications like corticosteroid cream, vitamins, etc.; physical therapy such hydrogel dressings, oxygen therapy, millimeter wave, etc.; and surgical procedures, etc. In Chinese medicine,

there is no specific term for radioactive skin damage, but radiation is a "fire" evil, and excessive fire-heat evil toxin accumulation leads to a number of manifestations of heat toxins in the skin coupled with damaged yin and fluids, which can be classified as "sores" and "burns" [19].Hu Hanqiong et al. [20] summarized data mining results and found that the TCM symptoms of radiation dermatitis are primarily classified as incandescent evil heat, Yin deficiency and toxicity, Qi stagnation and blood stasis, heat into the blood, heat and flesh decay, blood deficiency and fluid deficiency, damp-heat encapsulation, dry toxicity, and heat incandescent heart and lung. Comfrey, Borneol, Phellodendron, Coptis coptis, Rhubarb, Scutellaria, Licorice are the single herbs that are used the most commonly. Ointment, liquid, and oil are common dose forms used in TCM [21].

After radiation therapy, Pan Tingting et al. [22] enrolled 80 patients with lung cancer into observation group (n=40) and control group (n=40). The control group received standard care for radiotherapy side effects, whereas the observation group received To compare the skin improvement of the two groups, Nourishing Yin and Clearing Lung Soup (Astragalus membranaceus 40 g, Radix Ophiopogonis 20 g, endothelium corneum gigeriae galli 20 g, Suberect Spatholobus Stem 20 g, Angelica sinensis 20 g, Oldenlandia diffusa 15 g, edible tulip 15 g, radix pseudostellariae 12 g, Adenophora stricta 12 g, radices trichosanthis 12 g, Scutellaria baicalensis 10 g, Dan Pi 10 g, fried paeony 10 g, Licorice 5 g). The outcomes showed that Nourishing Yin and Clearing Lung Soup could significantly lessen lung cancer patients' post-radiation skin damage. Liu Xuejun [23] gathered patients undergoing radiotherapy for malignant tumors. The observation group included 19 cases of plus-flavored Si Miao Yong An cream combined with regular treatment, the control group, and: Results of 18 occurrences of placebo combined with usual therapy showed that plus-flavored Si Miao Yong An was effective. A cream might reduce the severity of acute radiological skin injury after it had already happened, prolong the time before it did, and enhance acute radiological skin injury prevention in patients receiving tumor radiation. It can delay the onset of radiation skin injury and has a superior preventative effect on acute radiation skin damage. Li Qiang [24] chose 50 patients with grade II-IV acute radiation skin injury, and the local wounds of the test group were treated with homemade traditional Chinese medicine ointment (made of 20g of Comfrey, 10g of draconis sanguis, 60g of Polygonum cuspidatum, 10g of borneol, 40g of angelica, 12g of cortex phellodendri, 30g of Radix Sanguisorbae, 500g of teal oil), and the local wounds of patients in the control group were treated with gentamicin combined with KangFuXinYe. The findings demonstrated that the herbal ointment manufactured could speed up the healing of wounds caused by acute radiological skin injuries. The intervention drug "Erhuang Decoction" spray was used in the experimental group, and the intervention drug triethanolamine cream was used in the control group. "Erhuang Decoction" is a seasoned formula by Prof. Lin Hongsheng for the treatment of radioactive skin injury using Chinese medicine, and it consists of three drugs, namely Coptis chinensis, cortex phellodendri and Polygonum cuspidatum. Qiao Hongli [25] selected malignant tumor patients with grade II-III radiation skin injury during or after radiotherapy. In comparison to triethanolamine cream, the study's findings demonstrated that "Erhuang Decoction" spray may more effectively treat localized skin lesions' edema, pain, and associated TCM clinical symptoms.

4. Radiation Esophagitis

A common side effect of radiotherapy for malignant tumors in the chest is radiation esophagitis, which typically presents as uncomfortable swallowing, dysphagia, acid reflux, a burning feeling behind the sternum, and in more severe cases, gastrointestinal bleeding and esophageal perforation. Modern medicine primarily focuses on anti-inflammatory, analgesic, and symptomatic management; therapeutic drugs include mucosal surface protectants, antibiotics (gentamicin),

anesthetics (lidocaine), vitamins (vitamin B12), and hormonal drugs (dexamethasone). These medications can improve patients' local symptoms and quality of life, but they are susceptible to side effects like immunosuppression and infection [26]. Radiation esophagitis falls under the category of "choking" in Chinese medicine. According to Professor Tong Li, the primary pathogenesis of radiation esophagitis is exposure to radiation "pathogenic dryness-heat," which can be further divided into phlegm and heat, fluid deficiency heat, internal obstruction of blood stasis, and spleen and kidney decline. Treatment for the disease's early stages is based on its symptoms, with a primary emphasis on clearing heat and detoxifying toxins, regulating and enhancing Qi flow, removing heat and phlegm, and reactivating blood circulation and dissolving blood stasis. The root deficit and mixed deficiency predominate in the later stage, which should be fed primarily by nourishing Yin and supplemented by eradicating evil [27].

Wang Hui et al [28] divided 60 patients with stage IIIB-IV non-small cell lung cancer treated radiotherapy for the first time into two groups, the control group received KangFuXinYe, and the treatment group received modified Zhi Bai Di Huang Tang (Poria cocos, Anemarrhena salti, cortex phellodendri, Rehmannia rehmanniae, Salt alisma, Rhizoma peony, cornus officinalis, Chinese yam, Paris polyphylla, Scutellaria baicalensis, Radix jasminoides, pseudostellaria heterophylla, radix ophiopogonis, Licorice), and the results showed that using modified Zhi Bai Di Huang Tang could lower the occurrence of radiation esophagitis and ameliorate symptoms. In a study by Zhang J et al [29], 122 patients with lung cancer or esophageal cancer who had received chest radiation were divided into a control group and a treatment group. Both groups received radiotherapy and chemotherapy, and patients in the treatment group started taking an oral peony root formula on the first day of radiotherapy. This formula contained 10 g of Radix Sophorae Tonkinensis, 30 g of radix paeoniae alba, 30 g of dandelion, 15g of gypsum, and 15 g of cordate houttuynia, licorice 10g, 15g of Chinese Starjasmine Stem, 15g of radix scrophulariae, 15g of bletilla striata, 3g of notoginseng powder, 0.3g of pearl, and 0.1g of borneol. When comparing the grading of radiation esophagitis at all levels before and after treatment in both groups, the study found that the proportion of grade 2 radiation esophagitis in the treatment group was considerably lower than that in the control group. Nini Zhao [30] collected 64 patients with central cancer treated with lung radiotherapy, and the test group started oral administration of Ji Zhi Bing Shao granule (rhizoma bletillae 30g, Dahurica 18g, borneol 1g, radix paeoniae alba 20g, honeysuckle 20g, fructus forsythiae 20g, adenophora stricta 20g, radix ophiopogonis 20g, rabdosia rubescens 30g, radix clematidis 20g, notoginseng powder 6g, colla corii asini 12g, and Acacia catechu 3g) on the day of radiotherapy until the end of radiotherapy. The results showed that the incidence of acute radiation esophagitis was reduced and the degree of clinical grading was reduced.

Radiation therapy is crucial in the treatment of lung cancer, but it is impossible to ignore its adverse effects, which can lead patients to suffer from physical and mental suffering and possibly end their course of treatment, which has an impact on the clinical effectiveness. Modern medicine primarily treats symptoms, which might lessen clinical symptoms, but the immunosuppression and subsequent infections that result can make follow-up treatment very challenging. Chinese medicine treatment is straightforward, practical, affordable, efficient, and safe. It can "prevent the disease before it happens, and prevent the disease before it happens," which can lessen the likelihood of radiation therapy side effects to some amount for patients with lung cancer. However, the most of the research on TCM treatment is centered on clinical experience and tiny samples, and it lacks a uniform standard. This is where our future efforts will be directed, based on homeland medicine, in order to better serve patients.

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