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Research Progress of Bazhen Decoction in the Prevention and Treatment of Qi and Blood Deficiency Syndrome Caused by Tumor Radiotherapy and Chemotherapy

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Abstract

The incidence of malignant tumors is increasing year by year. Due to the heterogeneity of tumors and the difference between early and late detection, surgical resection alone cannot meet the purpose of treatment. The treatment of malignant tumors is mainly based on surgery, combined with comprehensive treatments such as radiotherapy, chemotherapy, targeted therapy, and biological therapy. Radiotherapy and chemotherapy cannot accurately identify tumor cells and cause damage to human healthy tissues. Qi and blood deficiency syndrome is obvious. Traditional Chinese medicine is considered to be a treatment method with definite curative effect, mild effect and few side effects, and has gradually become a hot spot for adjuvant treatment of malignant tumors. Bazhen Decoction is a Chinese herbal formula composed of ginseng, Poriacocos, atractylodes macrocephala koidz, licorice, Angelica sinensis, Rehmannia glutinosa, Ligusticum chuanxiong Hort, and Radix Paeoniae Alba. This article reviews the related researches on modified Bazhen decoction in adjuvant treatment of malignant tumors, reducing the side effects of radiotherapy and chemotherapy, and improving the quality of life of patients.

Keywords: Bazhen Decoction; Qi and blood deficiency; Toxic and side effects; Traditional Chinese medicine treatment of malignant tumor; Microecology.

Introduction

Cancer is a major public health problem worldwide. According to the 2015 China Cancer Statistics released by Chen WQ [1] et al., the incidence of gastrointestinal tumors in men is second only to lung cancer and bronchial lung cancer; while the incidence of gastrointestinal tumors in women is After breast cancer and lung cancer, gastrointestinal cancer accounted for 45 of all cancer deaths in 2020, and the major cancer types in China have changed little in the past 5 years [2]. The difference in the distribution of this cancer type compared to developed countries results in a higher overall can cermortalityratein China, with approximately 22 of new cancer cases and 27 of cancer deaths globally occurring in China.

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Although the early screening of malignant tumors has achieved certain results, the overall situation is not optimistic. Most tumors have developed into the middle and late stages when they are discovered, and it is difficult ocure them by surgery at this time. Therefore, drug treatment is dominant in the treatment of middle and advanced tumors. Chemotherapy (chemotherapy) is the main treatment method for advanced malignant tumors. The efficacy of chemotherapy may vary among individuals due to different tumor heterogeneity, and the use of chemotherapy drugs may lead to related adverse reactions. According to statistics, about 70-80 of patients receiving chemotherapy experience different degrees of nausea and vomiting [3], and myelosuppression leads to thrombocytopenia (chemotherapy-induced thrombocytopenia, CIT), leukopenia and increased cytotoxicity [4,5], long-term chemotherapy will also cause symptoms of qi and blood deficiency such as light tongue coating, weak pulse, palpitations, insomnia, etc., which will not only affect the quality of life of patients, affect the confidence of patients in chemotherapy, but also reduce the compliance of patients with chemotherapy. Further chemotherapy was refused.

Traditional Chinese medicine is considered to be a therapeutic method with definite curative effect, mild miraculous effect and few side effects, and is increasingly important in the adjuvant treatment of malignant tumors.

Bazhen Decoction comes from "Zheng Ti Lei Yao", which is composed of ginseng, Poriacocos, atractylodes macrocephala koidz, licorice, Angelica sinensis, Rehmannia glutinosa, Ligusticum chuanxiong Hort, and Radix Paeoniae Alba. The people in the recipe participate in the matching of Rehmannia glutinosa, nourishing Qi and nourishing blood, and they are the monarch medicines; atractylodes macrocephala koidz, Poriacocos, invigorating the spleen, invigorating the spleen, and helping ginseng to nourish the spleen; Angelica sinensis and Radix Paeoniae Alba nourish the blood and nourishment, and help the Rehmannia glutinosa nourish the heart and liver. They are all ministerial medicines. Ligusticum chuanxiong Hort as the assistant, activating blood and promoting qi, so that Rehmannia glutinosa, Angelica sinensis, Radix Paeoniae Albatonic but not stagnant; licorice as the ambassador, invigorating Qi and neutralizing, reconciling various medicines. Bazhen Decoction is a combination of Sijunzi Decoction and Siwu Decoction. Sijunzi Decoction can strengthen the spleen and Qi, and Bazhen Decoction combines the characteristics of the two. In the past, it was used to treat Qi and blood deficiency, and now it is also used to improve hematopoietic function, improve immunity, promote wound healing, and prevent and treat toxic and side effects of tumor radio therapy and chemotherapy.

Studies have shown that Bazhen Decoction can improve patients' immunity and reduce chemotherapy-related adverse reactions in adjuvant treatment of malignant tumors. Therefore, Bazhen Decoction as a traditional Chinese medicine plays an important role in the adjuvant treatment of malignant tumors. Siwu Decoction can nourish and nourish blood.

Clinical application of modified bazhen decoction in the prevention and treatment of toxic and side effects of tumor chemotherapy

Gastro intestinal reactions are common adverse reactions of chemotherapy, manifested as nausea, vomiting, poorappetite, constipation, abdominal distension, etc. Repeated nausea and vomiting can cause water and electrolyte disorders, malabsorption, malnutrition, etc. life. He Yuqing [6] enrolled 44 patients with gastric cancer after chemotherapy. The control group was given conventional western medicine for antiemetic and acid suppression, and the treatment group was given Bazhen Decoction. The results showed that the incidence of severe vomiting in the treatment group was lower than that in the observation group. Wang Hongyu [7] enrolled 70 patients with platinum-based chemotherapy. The treatment group received adjuvant chemotherapy with modified Bazhen Decoction, and the control group received conventional chemotherapy. The results showed that the toxic and side effects of chemotherapy and gastrointestinal symptoms in the treatment group were lower than those in the control group. Ren P [8] et al. have confirmed that Bazhen Decoction can improve gastric electromotor and regulate the levels of Motilium (MOT), Cholecystokinin (CCK) and Somatostatin (SS) in the hypothalamus. The gastric juice of the ratis emptied, thereby reducing the corresponding gastro intestinal symptoms of the patient. The studies of C,Q, Yi [9] and others further confirmed that it can correct a certain degree of small intestinal digestion and absorption function, and auxiliary enteral nutrition can improve the patient's condition[10].

Bazhen decoction adjuvant chemotherapy can also alleviate other adverse reactions caused by malignant tumors or chemotherapy. It has been reported [11] that Bazhen Decoction can improve the symptoms of qi and blood deficiency caused by chemotherapy, such as nervous exhaustion, palpitations, shortness of breath, dizziness, pale complexion, chills, anorexia, etc., and relieve peripheral nerve damage caused by hands and feet. Numbness [12]. In addition, many studies have shown that modified Bazhen Decoction can improve post operative pain associated with malignant tumors [13,14]. "Nonourishesis pain" is one of the important perspectives of Chinese medicine theory to understand pain, and in Bazhen Decoction, Siwu Decoction composed of Angelica sinensis, Rehmannia glutinosa, Ligusticum chuanxiong Hort, and Radix Paeoniae Alba is good at nourishing blood. Through the chemotherapy-induced blood deficiency rat model, it was found that Siwu Decoction protects the hematopoietic function of the bone marrow through the TLR4/NF-κB/NLRP3 pathway, and improves the anemia caused by chemotherapy [15], and the symptoms of blood deficiency such as fatigue, shortness of breath, dizziness, anorexia, and pain were relieved. Decoction composed of Angelica sinensis, Rehmannia glutinosa, Ligusticum chuanxiong Hort, and Radix Paeoniae Alba is good at nourishing blood. Through the chemotherapy-induced blood deficiency rat model, it was found that Siwu Decoction protects the hematopoietic function of the bone marrow through the TLR4/NF-κB/NLRP3 pathway, and improves the anemia caused by chemotherapy [15]., and the symptoms of blood deficiency such as fatigue, shortness of breath, dizziness, anorexia, and pain were relieved.

Study on the mechanism of adjuvant treatment of tumor with bazhen decoction

Domestic scholars have found through a mouse model of liver cancer that the tumor volume of mice with Qi deficiency syndrome is significantly larger than that of control mice, and the a typical proliferation of tumor cells is more significant. This study suggests that Qi deficiency syndrome may be one of the factors

that promote tumor progression [16], therefore, Bazhen Decoction, which has the function of tonifying qi and blood and supporting righteousness, can curb the progression of tumors to a certain extent. The research from the perspectives of active ingredients and signaling pathways has carried out a more detailed exploration of the mechanism of Bazhen Decoction's efficacy and detoxification.

According to the research report of LIUY [17] and others, after decoction of ginseng and licoricein Bazhen Decoction, the active ingredients are ginsenosides, flavonoids and triterpenoids. Triterpenoids have antiviral activity [18-20], licorice and its derivatives can prevent DNA damage caused by carcinogens, glycyrrhizic acidc and own regulate proteinkinase C, down-regulate epidermal growth factor receptor, and licoricepolyphenols can induce apoptos is in cancer cells [21,22]. Flavonoids can inhibit the NF-KB cell survival signaling pathway and induce apoptosis and cell death of liver cancer cells [23]. Zeng Meifang et al., [24] found that Bazhen Decoction combined with Xiaoyao Powder could regulate the ERK/MAPK signaling pathway by up-regulating the expression of MAP3K1, FODX3, KLF4 protein and down-regulating the expression of SOX2 protein, there by inhibiting the growth of tumor cells. Bazhen Decoction can inhibit breast cancer angiogenesis, and its mechanism may be related to the inhibition of VEGF (Vascular Endothelial Growth Factor) expression in breast cancer tissue [25]. Zhao, AG [26] et al. used human gastric cancer cells transplanted into nude mice as a model and found that the intervention of Sijunzi Decoction-based prescriptions could inhibit the growth of gastric cancer in nude mice, and this inhibition may be related top 53 and bcl-2 low expression.

Modulation of bazhen decoction on the immune system

Liu Chunying [27] and others used Bazhen Decoction to improve the anti-tumor ability by improving the activity of NK cells, increasing the level of IL-2 and enhancing the phagocytic ability of peritoneal macrophages. And the effect of compound decoction is better than that of single prescription.

Adjuvant chemo radio therapy can kill tumor cells and damage normal cells, especially cells that are actively renewed. The most common one is myelosuppression. Zhao Yiqing [28] and others used 60 Co gamma-ray to irradiate the whole body of mice to dynamically observe the apoptosis of bone marrow cells and spleen cells. The results showed that the number of apoptosis of bone marrow cells and spleen cells in the Bazhen Decoction group was smaller than that in the model group. There were significant differences in mice at 6h, 12h, 18h, and 24h, that is, Bazhen Decoction had a good inhibitory effect on the apoptosis of bone marrow cells and spleen cells in mice irradiated with 60Co gamma rays. Another study confirmed that Bazhen Decoction can activate spleen cells [29]. Chun Ze [30] confirmed that Bazhen Decoction has a pro-proliferation effect on bone marrow cells in the study of Bazhen Decoction on cyclophosphamide-induced myelo suppression in mice, which may be by directly or indirectly stimulating the matrix of the hematopoietic microenvironment The cells secrete positive or negative hematopoietic growth factors to achieve the realization, and the compatibility of S. chinens is can also play a role in reversing and promoting the reversal of myelosuppression [31]. Using Bazhen Decoction to intervene, it was found that different concentrations of Bazhen Decoction can promote the proliferation of T lymphocytes at different times, and it is positively correlated with the action time and concentration course, and has the same secretory effect on the secretion of IFN-γ and IL-2. It can regulate inflammatory factors, improve immune function, stimulate the transcription of Erythropoietin (EPO) in the kidney, and the proliferation and activation of T cells have antioxidant and anti-tumor effects [32-37].

Effects of modified bazhen decoction on microecology

Studies have found that the rare differences in the intestinal flora of Qi deficiency syndrome and normal people. The former has increased abundance of Sphingolipids, Clostridium, and Combustomonas, but lacks probiotics such as Bifido bacterium and Hirudovibrio and bacteria that suppress inflammatory responses [38]. The interaction between Qi and blood deficiency syndrome and intestinal flora may be one of the influencing factors of disease outcome, and many studies have confirmed the effect of Bazhen Decoction and its components on intestinal microecology.

Geng, J [39] et al. showed that supplementation of Modified Bazhen Powder (MBP) in lactating sow diets increased the microbial diversity in sow colostrum and transition milk. Airy products were dominated by Proteo bacteria and Firmicutes at the phylum level in the control group and MBP group. The number of Firmicutes decreased in the MBP group while the abundance of Proteo bacteria was relatively increased. At the genus level, Enterococcus and anaerobes were in Relative abundance was significantly reduced in pig milk and affected metabolomic changes. Zhu Min et al., [40] used tripterygiumwil for diipoly glycosides to establish rats with low ovarian function, and divided them into blank group, model group, Siwu Decoction high-dose group and Siwu Decoction low-dose group, respectively. The diversity of intestinal flora was restored, the content of beneficial bacteria was increased, and the composition of intestinal flora was shifted to normal rats. Li, Wang yang et al. [41] found that Taohong Siwu Decoction could regulate the intestinal microbiota of rats, and the abundance of Bacteroidetes and Firmicutes increased, showing a positive regulatory effect of the two to a certain extent.

Discussion and prospects

Bazhen Decoction, as a classic prescription for qi and blood supplementation, integrates the curative effects of Sijunzi Decoction and Siwu Decoction. It has a significant effect on gastrointestinal reactions caused by chemotherapy, and can improve the anti-tumor effect, promote tumor cell apoptosis, and relieve chemotherapy. The resulting syndrome of qi and blood deficiency can improve bone marrow suppression, improve immunity and the quality of life of patients, and affect the distribution and abundance of flora in the body. At present, traditional Chinese medicine is being paid more and more attention as an adjuvant drug for radiotherapy and chemotherapy. It has many effects that cannot be explained by western medicine, and the mechanism is not understood. For example, the active ingredients in Bazhen Decoction that exert pharmacological effects are not yet clear, and more research is needed to prove its mechanism of action. It is expected to play a role in more disease fields and provide a basis for new drug development, dosage Form reform and clinical application.

Declarations

Conflict of interest: We have no conflicts of interest to disclose.

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