The Analysis of the Adverse Reaction of Traditional Chinese Medicine Tumor Bone Marrow Suppression

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Abstract. With the rapid increase of cancer patients, chemotherapy is the main method for the clinical treatment of cancer, but also in the treatment of the adverse reactions--bone marrow suppression is often a serious infection caused by patients after chemotherapy and the important cause of mortality. Chinese medicine has obvious advantages in the prevention and treatment of bone marrow depression after chemotherapy. According to tumor bone marrow suppression after chemotherapy of etiology and pathogenesis of traditional Chinese medicine and China national knowledge internet nearly 10 years of traditional Chinese medicine in the prevention and control of the status of clinical and laboratory research of tumor bone marrow suppression, the author analyzed and summarized its characteristics, so as to provide the basis for treating bone marrow suppression of drug research and development, and promote small adverse reactions of the development and utilization of natural medicine and its preparations.

1. Introduction
China has become the world's second largest cancer producer, with 2.2 million new cancer patients each year, accounting for about 20 percent of all cancer patients in the world. According to data statistics, in the course of tumor radiotherapy and chemotherapy 80% of patients will have bone marrow suppression. Modern medical treatments for myelosuppression include hematopoietic cell colony factor, component transfusion, and elevated leucocyte drug and small-dose hormone therapy [1]. In recent years, Traditional Chinese Medicine (TCM) in the prevention and treatment of chemotherapy caused by bone marrow suppression has achieved remarkable results, Chinese medicine can adjust the body function, so that the body organs, blood, yin and yang function balance, syndrome differentiation with a permanent effect [2]. Therefore, in this paper, according to tumor bone marrow suppression after chemotherapy of etiology and pathogenesis of TCM and China national knowledge internet(CNKI) nearly 10 years of traditional Chinese medicine in the prevention and control of the status of clinical and laboratory research of tumor bone marrow suppression and analysis the characteristics of Chinese medicine in clinical application. It will provide some guidance for the research and development of clinical diagnosis and treatment of bone marrow suppression.

2. Etiology and Pathogenesis of Chinese Medicine in Bone Marrow Suppression after Tumor Chemotherapy
TCM ancient books and records without bone marrow suppression, most scholars according to its characteristics of symptoms to be classified as "consumptive disease" “deficiency of blood” and other areas. They believe that chemotherapy drugs are exogenous pathogenic agents, which can damage the body and lead to dysfunction of viscera, showing Qi and blood damage, liver-kidney deficiency, weakness of the spleen and stomach and other syndromes. Therefore, according to the principle of
TCM syndrome differentiation and treatment, the treatment of bone marrow suppression should be based on the basic principle of strengthening the body resistance, mainly benefiting qi and nourishing blood and invigorating the kidney and strengthening the spleen; In addition, Chinese medicine believes that "blood stasis does not go, then the new blood is not born". Deficiency of Qi and blood will cause blood stasis, it can also be used to activate blood circulation to dissipate blood stasis, from Qi and blood, spleen, kidney, blood stasis and other aspects of prevention and treatment.

3. Overview of Modern Research on Bone Marrow Suppression after Chemotherapy

In recent years, traditional Chinese medicine has made some progress in preventing and controlling the adverse reaction of bone marrow after chemotherapy, which has obvious advantages and outstanding effect. Review China national knowledge internet 2007-2017 research in traditional Chinese medicine in the prevention and treatment of tumor bone marrow suppression, search keywords "tumor", "bone marrow suppression" retrieved a total of 247 literatures(excluding doctoral thesis, master thesis, reviews, descriptive article), in the 247 paper, clinical application research with 170 references, 77 pieces of laboratory research. Through the analysis of 170 papers on clinical application, it was found that the prevention and treatment of the adverse effects of bone marrow suppression in Chinese medicine mostly started from Qi and blood, spleen and kidney, and treated by syndrome differentiation. Prevention and treatment methods are both internal and external therapies. According to the etiology and pathogenesis of bone marrow suppression, the related literature of clinical treatment can be divided into the internal treatment method: benefiting qi and nourishing blood and invigorating the kidney and strengthening the spleen. There are other therapy of activate blood circulation to dissipate blood stasis to treat tumor marrow suppression. Internal treatment includes single drug, traditional prescription, Chinese patent medicine and active ingredient of traditional Chinese medicine. External treatment, treatment by acupuncture point is also more widely used in clinic. There are 29 literatures about acupuncture treatment and there are 27 literatures on the prevention and treatment of Chinese medicine injection. Acupuncture point injection combined with acupuncture and medicine, although the research is relatively few, but the curative effect is reliable and the prospect is broad.

4. Clinical Application of Chinese Medicine in the Prevention and Treatment of Tumor Marrow Suppression

4.1. Benefiting qi and Nourishing Blood
Chinese medicine for bone marrow suppression adverse reactions prevention and treatment of clinical research, there are 79 literatures about the treatment of benefiting Qi and blood. Chinese medicine believes that bone marrow suppression belongs to "consumptive disease" "deficiency of blood"and other areas, it can damage the body Qi and blood. The two deficiency of qi and blood are the common syndromes of bone marrow suppression after chemotherapy, The clinical symptoms are fatigue, sweating, palpitation and shortness of breath, pale tongue, thin and weak pulse and other symptoms [3]; Qi and blood are breeding with each other, Qi deficiency is less blood, less blood is Qi deficiency, so in the Chinese medicine clinical, mostly Qi and blood double supplementation. Shenqi Shiyiwei Granule, It is a combination of Chinese medicinal herbs, such as angelica, wolfberry, astragalus, cassia, antler and ginseng, etc. Xie Huiliang used Shenqi Shiyiwei Granule preventing 131I induced bone marrow suppression therapy for differentiated thyroid carcinoma, with benefiting Qi and blood, tonifying Qi and lifting yang, which can inhibit the growth of cancer cells, prevent cancer patients on chemotherapy induced toxicity and adverse reactions, promote the restoration of the generation and hematopoietic function of white blood cells[4-5]. Zhang Yipeng adopted in clinical Fu Yang Sheng Xue Paste Recipe for prevention and treatment of tumor bone marrow suppression caused by chemotherapy, which are relevant to syndromes and pathogenesis of patients, tonifying qi and blood supplementing, it can improve the clinical symptoms of patients with chemotherapy, improve the quality of life of patients[6].

4.2. Invigorating the Kidney and Strengthening the Spleen
Chinese medicine believes that chemotherapy drugs vulnerable to the kidney, so patients after chemotherapy is not only the two most deficiency of both qi and blood, the vast majority of both kidney
deficiency. Spleen kidney deficiency is the pathological basis of bone marrow suppression after chemotherapy. The kidney being the origin of congenital constitution, the source of blood lies in the kidney; the spleen being the foundation of acquired constitution, the source of Qi and blood; It is more common to have kidney deficiency, such as painful waist and knee pain, facial complexion, dizziness and tinnitus. Jianpi Bushen Paste can invigorate the spleen and kidney, have obvious bone marrow protection effect, restore the function of bone marrow, and improve the clinical symptoms of the patients, enhance immunity [7]. In the relevant clinical literature, there are 35 articles from the spleen and kidney to prevent bone marrow suppression, it commonly used drugs are Radix Rehmanniae Preparata, Ligustrum lucidum, Psorslea corylifolia L., Chinese yam etc..

4.3. Activating Blood Circulation to Dissipate Blood Stasis
Qi stagnation, blood stasis, and phlegm-retention are the main pathological mechanisms of cancer. The occurrence of tumor is also related to the disorder of human body, diet, tiredness and so on, the human body for a long time in this state will cause the imbalance of yin and Yang, viscera imbalance and combination of cancer toxin and blood stasis. Chemotherapy drugs in the treatment of tumors at the same time, increased the combination of cancer toxin and blood stasis, and thus derived from a variety of complications. It is also a new direction for future research to treat the adverse effects of bone marrow suppression by activating blood circulation to dissipate blood stasis [8]. Sanyang Xuedai Mixture of Dai medicine composed of ginger, dragons blood, pseudo-ginseng etc., It has the effect of invigorating spleen, producing blood, removing stasis and producing new. It can antagonize radiotherapy and chemotherapy, protect bone marrow hematopoietic function and improve the sensitivity of radiotherapy. For the concurrent chemoradiotherapy of head and neck squamous cell carcinoma, it can reduce the degree of bone marrow suppression, delay the occurrence of bone marrow suppression, and promote the recovery of bone marrow suppression [9].

4.4. Acupoint
Acupuncture point is a peculiar term of Chinese traditional medicine. Chinese medicine can cure diseases by acupuncture or massage, point by point and moxibustion. At present, there are 29 literatures about the prevention and treatment of tumor myelosuppression by using acupoint, and some achievements have been achieved. The clinical malignant tumor patients use traditional Chinese medicine plaster Acupoint Moxibustion Therapy and hot compress method, which can stimulate acupoints having the function of promoting hematopoiesis of bone marrow. Results after chemotherapy, there were no significant differences in leukocyte, neutrophil, and platelet levels compared with those before chemotherapy [10]. Acupoint catgut embedding also has the effect of reducing leukocytes and neutrophils caused by chemotherapy drugs. The clinical literature mainly by stimulating Shenshu, Zusanli point, protects the bone marrow hematopoietic function and improves the ability of tolerance of chemotherapy.

4.5. Chinese Medicine Injection
The traditional Chinese medicine injection can be used with chemotherapy drugs to protect the bone marrow and improve the hematopoietic function of bone marrow. In clinical studies, there are 27 literatures about Chinese traditional medicine injection. The commonly used traditional Chinese medicine injections include Shenfu injection, Shenmai injection, astragalus injection and Shengmai injection. Studies have shown that Shenfu injection can reduce the chemotherapy drug taxol, vinorelbine and gemcitabine combined with TAC regimen in the treatment of breast cancer of the bone marrow inhibition and digestive tract symptoms; for patients with breast cancer, the incidence of adverse reactions after application of Shenfu injection decreased significantly[11]. The use of Shenmai injection in the prevention and treatment of docetaxel bone marrow suppression can significantly reduce the myelosuppression and toxicity of chemotherapeutic drugs after chemotherapy [12]. Shengmai injection has obvious preventive and therapeutic effect on bone marrow suppression in chemotherapy of malignant tumor, and can also alleviate the toxicity of chemotherapy in patients with advanced tumor [13].
4.6. Combination of Acupuncture Point and Chinese Medicine Injection

Acupuncture injection combined acupuncture with medicine is relatively small in clinical practice, but its efficacy is reliable. Most of the acupuncture point injection at Zusanli point, which has the effect of regulating spleen and stomach, tonifying middle-Jiao and Qi and strengthening the body resistance to eliminate pathogenic factors. Acupoint injection of Astragalus injection at Zusanli point can effectively improve the bone marrow suppression in patients with ovarian cancer chemotherapy [14].

5. Laboratory Study on Prevention and Treatment of Tumor Bone Marrow Suppression with Chinese Medicine

Of the 2007-2017 studies on tumor marrow suppression in CNKI, 77 were laboratory animal models. The animals were basically different methods for the bone marrow suppression model mice, and only 5 were made in rats. The drugs used for TCM extract relates to the extraction of active ingredients from Sanguisorba officinalis, Herba Rhodiolae, ginseng and other herbs, it also have the traditional prescription and Chinese medicine (Xiaoyantang, DiyuShengbaipian, Zuoguiwan etc.). There are some related literatures to investigate the effect of acupuncture on bone marrow suppression mice, and the research direction is mainly on the hematopoietic system and immune system of bone marrow suppression mice.

The laboratory used lethal doses of cyclophosphamide peritoneal injection to make bone marrow suppression mice model. The angelica polysaccharides and compatibility of astragalus polysaccharides treatment, the results show that the astragalus polysaccharides and angelica sinensis polysaccharide combination can promote bone marrow inhibition in vitro proliferation and differentiation of hematopoietic stem cells in mice and the secretion of cytokines. Yang peiying inoculates the Lewis lung cancer tumor strain into mice to explore the effect of c on bone marrow suppression of mice with Lewis lung cancer after chemotherapy. Results showed that Xiaoyan Decoction combined with rh G-CS can improve the level of WBC and immunological functions of peripheral blood in bone marrow suppression model mice. And the effect of combination of both drugs is more significant[15]. Lu Mei on myelosuppressed mice selected "Dazhui", "Ge Shu", "Shenshu" and "Zusanli" respectively by Acupuncture and moxibustion treatment. Results showed that Acupuncture and moxibustion can improve the content of GM-CSF and G-CSF CTX in sera of mice. Promoting the proliferation and differentiation of bone marrow hematopoietic cells, so as to facilitate the reconstruction of bone marrow hematopoietic function, reduce the alkylating agent bone marrow inhibition caused by CTX, thereby improving peripheral blood leukocytes[16].

6. Outlook

Although compared with western medicine, traditional Chinese medicine has a slow effect, but it plays a therapeutic effect from multiple links and multiple targets. According to the tumor patients with bone marrow suppression of etiology and pathogenesis and the characteristics of bone marrow suppression after chemotherapy, adopt corresponding method in the treatment, treatment from the qi and blood, spleen and kidney, nourishing qi and blood, spleen and kidney simultaneously, not only alleviate the patient's clinical symptoms, improve quality of life, improve cancer lesions and prolong their life, it can also adjust the body's inherent ability of disease resistance, disease prevention, control the development of cancer prevention and treatment of tumor patients with help.

Both western medicine and traditional Chinese medicine have made remarkable progress in the research and treatment of bone marrow suppression mechanism, but there are still some unresolved problems. For example, most studies have focused on the treatment of bone marrow suppression after chemotherapy, and have less research on the prevention of bone marrow suppression caused by chemotherapy; Most studies of traditional Chinese medicine are limited to clinical application, more in-depth and systematic pharmacological and toxicological studies are rare, and many reports of clinical samples are too small, the standard of efficacy is not standardized, lack of persuasion; The observation indexes were limited, mostly white blood cells, hemoglobin, platelet count, and no new persuasive index was found; In laboratory studies, the experimental animal basically for mice, rats, no other strains of animal research, whether to expand the scope of the study, and the research direction is basically the study of hematopoietic and immune systems, the research direction is single.
In view of the above problems, there is still a great room for further research on bone marrow suppression in Chinese medicine in the future. In the treatment of traditional Chinese medicine, it can further play the preventive role of Chinese medicine in the occurrence of bone marrow suppression after chemotherapy; In the clinical application of the treatment, dig their effects of systematic pharmacological and toxicological mechanism, and expand the scope on the basis of previous studies, using the research methods of large sample, multicenter, randomized and controlled; To find more persuasive observation indicators, when conducting laboratory research, we can innovate in many directions from different angles and find new treatment pathways. It is believed that with the continuous development of science and technology and the continuous development of clinical research, the potential of traditional Chinese medicine in the field of preventing and controlling the adverse reactions of tumor marrow is limitless.

7. Acknowledgment
This research was financially supported by the national international cooperation base (2016-65), the Central Plains scholars (162101510003)

8. References
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