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A Minireview on the Supportive Care in Cancer with Traditional Chinese Medicine

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ABSTRACT

Traditional medicine has been applied in cancer treatment in many countries for a long time. Among the various forms of complementary and alternative medicine, traditional Chinese medicine has a well constructed theoretical framework and established treatment approaches. Recent research has displayed that the traditional Chinese medicine is effective in the supportive cancer care in neoadjuvant and adjuvant chemotherapy. In this study, the clinical trials results of traditional Chinese medicines currently conducted in clinical practice in China.

Key words: Supportive care, cancer, traditional Chinese medicine

INTRODUCTION

A lot of cancer patients in the Western countries have utilized some forms of Complementary and Alternative Medicine (CAM) to support their conventional cancer therapies (Ben-Arye *et al.*, 2014). Among the various forms of CAM, Traditional Chinese Medicine (TCM) is one of the few that has a well constructed theoretical framework and established treatment approaches for diseases including cancer (Wong *et al.*, 2001). The use of TCM for the management of cancers can be traced back to Shang Dynasty of 3500 years ago. Over the centuries, various TCM therapeutic interventions have been developed and employed in cancer treatment (Cho, 2010; McQuade *et al.*, 2012; Xu *et al.*, 2013). There has been a substantial increase in Randomized Controlled Trials (RCTs) over the past three decades. In this study, some lines of scientific evidence are reviewed.

MODULATING IMMUNE FUNCTION

The development of a clinically apparent cancer is due, in part, to the failure of the immune system to adequately recognize and dispose of the initial malignant cells. Thus, cancer may be regarded as an immune system failure (Wang *et al.*, 2012). The ideal anticancer treatment would not only attack the cancer cells directly, it should support the immune system's efforts to eliminate any stray malignant cells. Astragalus root is a common herb with well-documented

immune-modulating properties (Geng, 1986). A potent bioactive fraction isolated from astragalus root demonstrated varied immune stimulating actions, both *in vitro* and *in vivo*. Specifically, macrophage number and phagocytic activity were increased, IL-2 expression was enhanced and tumors in murine models were suppressed. Other studies also revealed that a decoction containing astragalus root induced secretion of IL-2 and regulated macrophage immune response (Chen, 1994). Regulatory T cells play a role in host homeostasis, inhibiting the host anticancer immunization. The CD4+CD25+ Treg cells from cancer patients are higher than that of healthy people. To neutralize CD4+CD25+ Treg cells in cancer patients would enhance the efficacy of anticancer immunization (Roux *et al.*, 2008).

Fuzheng yiliu ointment: A head-to-head study compared the effect of Fuzheng Yiliu Ointment and Zhenqi Fuzheng Granules on spleen-deficiency syndrome after adjuvant chemotherapy in colorectal cancer. Fuzheng Yiliu Ointment consists of Astragalus membranaceus (huangqi), American ginseng (xiyangshen), Chinese yam (shanyao) and Poria (fuling) primarily. Zhenqi Fuzheng Granules consist of Astragalus membranaceus (huangqi) and Ligustrum lucidum (nvzhenzi) primarily. Forty cancer patients were randomly assigned to 2 groups. Both were administered for 4 weeks. In both group the CD4+CD25+ Treg cells in peripheral blood were significantly lowered at the end of 4 weeks administration of TCM, meanwhile the levels of Tumor

Necrosis Factor- α (TNF α) and interleukin-12 (IL-12) were increased significantly. Moreover, the integral of TCM syndromes and toxic reaction were reduced after treatment in both groups. In general, Fuzheng Yiliu Ointment is superior to Zhenqi Fuzheng Granules in regulating the immune function, reducing the adverse reaction of chemotherapy in colorectal cancer patients (Lv *et al.*, 2014).

Kang-ai injection: Kang-ai Injection was made from *Astragalus membranaceus* (huangqi), *Panax ginseng* (renshen), and which can strengthen vital-qi. Effect on immunological function and Quality of Life (QoL) of Kang-ai Injection in advanced NSCLC patients' chemotherapy were investigated. A total 83 lung cancer patients were randomized into combination group and control group. Combination group was Kang-ai Injection plus NP regimen (vinorelbine+cisplatin) and control group just used NP regimen. After 2 cycles of chemotherapy, the effective powers were 61% in combination group and 31% in control group, respectively, with significant difference ($p < 0.01$). The CD3+, CD4+ and CD4+/CD8+ were increased significantly in combination group compared to those in control group; meanwhile CD8+ was reduced significantly in combination group compared to that in control group. The general health status in combination group was obviously better than that in control group. Therefore, Kang-ai Injection could enhance immunological function of lung cancer patient (Chen, 2014).

Shenqi fuzheng injection: Shenqi Fuzheng Injection was extract of *Astragalus membranaceus* root (huangqi) and *Codonopsis pilosula* (dangshen). Forty colorectal cancer patients were randomly assigned into 2 groups. The control group received chemotherapy of FOLFOX protocol and the other group was added Shenqi Fuzheng Injection to chemotherapy. After treatment, the amounts of CD4+CD25+ Treg cell in Shenqi Fuzheng Injection group were lower significant than control group, which suggested that Shenqi Fuzheng Injection might modulate the Treg cells and enhance the anticancer efficacy (Zhang *et al.*, 2011). Moreover, Shenqi Fuzheng Injection significantly reduced the frequency of nausea and vomiting due to chemotherapy, reduced the incidence of clinically significant leucopenia.

INCREASING POTENCY AND REDUCING TOXICITY IN NEOADJUVANT CHEMOTHERAPY

Evidences show that integrating Chinese and Western medicine may usually improve survival outcomes through increasing potency and reducing toxicity of chemotherapy, both in neoadjuvant chemotherapy and adjuvant chemotherapy (Sagar and Wong, 2008).

Fukangling granules: Fukangling Granules is empirical TCM prescription consisted of *Astragalus membranaceus* (huangqi), *Poria* (fuling) and *Ligustrum lucidum* (nvzhenzi). Breast cancer patients administrated Fukangling Granules in combination with neoadjuvant chemotherapy displayed higher

remission rate (72%) as compared to patients administrated with simple neoadjuvant chemotherapy (45%) (Li *et al.*, 2010).

Jinlong capsule: Jinlong Capsule (JLC) is made from 3 kinds of reptiles, Fresh gecko (*xianshougong*), Fresh *Bungarus parvus* (*xian jinqian baihuashe*), and Fresh *Agkistrodon acutus* (*xian jishe*). In TCM practice, JLC can support vital-qi. A RCT analyzed the therapeutic efficacy and adverse reaction induced by JLC combined with TEC regimen (docetaxel+epirubicin+cyclophosphamide) in neoadjuvant chemotherapy in breast cancer patients. A total of 64 patients who had stage II to III breast cancer were divided into 2 groups randomly: JLC combined with neoadjuvant chemotherapy group (JLC group) and conventional neoadjuvant chemotherapy group (control group). The chemotherapy cycle was 21 days. Evaluations of therapeutic effects were made after 3 cycles of neoadjuvant chemotherapy and consequent operation. The results displayed that the effective power (complete response+ partial response) of the JLC group and the control group were 84 and 56% respectively, with significant difference ($p < 0.05$). The main adverse effects were grades II to III gastrointestinal tract reactions and myelosuppression. WBC decrease and incidence rate of nausea/vomiting were obviously lower in the JLC group than in the control group ($p < 0.05$). The QoL of patients in the JLC group was greatly improved than that in the control group ($p < 0.05$). In general, the application of JLC combined with neoadjuvant chemotherapy can improve therapeutic efficacy and reduce the toxicity of chemotherapy, thereby improving the life quality of patients (Bai and Wu, 2014).

Kanglaite injection: Kanglaite injection was made from Coix seed extract. Seventy seven breast cancer patients were divided into 2 groups randomly, Kanglaite plus neoadjuvant chemotherapy group and simple chemotherapy control group. Therapeutic efficacy was evaluated after 3 cycles of chemotherapy and consequent operation. The complete response and partial response rates of Kanglaite group and control group were 81 and 48%, respectively, with significant difference ($p < 0.05$). The WBC counts decrease, nausea and vomiting were obviously slighter in Kanglaite group than in control group. The QoL of patients in Kanglaite group was greatly improved compared to control group (Gan *et al.*, 2009).

Tao-hong Si-wu decoction: Tao-hong Si-wu decoction is a classical prescription for activating blood circulation to remove stasis (*huo xue hua yu*). It was composed by Peach kernel (*taoren*), Rhizome of *Chuanxiong* (*chuanxiong*), *Radix Paeoniae Alba* (*baishao*), *Safflower* (*honghua*), *Chinese Angelica* (*danggui*) and *Radix Rehmanniae Preparata* (*shudihuang*). Seventy eight breast cancer patients were randomized into 2 groups. One group was given Tao-hong Si-wu decoction combined with neoadjuvant chemotherapy, and the other was given neoadjuvant chemotherapy as control. The results showed that after administration with Tao-hong Si-wu decoction, the physiological status, emotional

status, functional status and QoL score were improved significantly as compared to control group. In addition, Tao-hong Si-wu Decoction could decrease incidence of digestive tract reaction, alopecia, and bone marrow suppression (Dong, 2014).

INCREASING POTENCY AND REDUCING TOXICITY IN ADJUVANT CHEMOTHERAPY

GongKang decoction: A RCT investigated the effect of GongKang Decoction on postoperative chemotherapy in 96 endometrial cancer patients (Zhang *et al.*, 2014). GongKang decoction was primarily made from *Astragalus membranaceus* (huangqi) and *Codonopsis pilosula* (dangshen). After administration of GongKang Decoction for 3 months, the WBC counts, QoL score and 5-year survival rate were significantly increased in the combination group (GongKang Decoction plus conventional chemotherapy) compared to conventional chemotherapy alone group. Meanwhile the gastrointestinal side-effects, pain score and 5-year recurrence rate were significantly reduced in the combination group than conventional chemotherapy alone group.

Jianpi Yiqi decoction: Jianpi Yiqi decoction was made from *Codonopsis pilosula* (dangshen), *Rhizoma atractylodis macrocephalae* (baishu), and *Poria* (fuling) primarily. Seventy eight advance colorectal cancer patients were randomly divided into 2 groups. In control group patients only received chemotherapy while in test group the patients were added Jianpi Yiqi Decoction. The short-term response rates were similar between 2 groups, however, the incidence of systemic adverse reactions was lower in test group than in control group, and the QoL score was higher in test group than in control group (Li *et al.*, 2012).

Kang-ai injection: As one of the most commonly used TCM in cancer treatment, Kang-ai Injection was also applied in breast cancer patients' postoperative chemotherapy. A total of 96 breast cancer patients after operation were randomized into 2 groups, experimental group (postoperative chemotherapy plus Kang-ai Injection) and control group (simple postoperative chemotherapy). After the 4 cycles of treatment, life quality in experimental group was superior to that in control group, with significant difference ($p < 0.05$). The WBC decrease and CA-153 levels were significantly lower in control group than those in experimental group. The data means that Kang-ai Injection in combination with postoperative chemotherapy can improve the QoL of patients and reduce bone marrow suppression (Wu, 2010).

Stove subsoil: Stove subsoil is a brown soil from a common firewood stove in rural area in the north of China. In TCM practice, Stove subsoil has been applied for bleeding, vomiting and diarrhea. A head-to-head clinical study investigated the effect of Stove subsoil on gastrointestinal reactions following tumor postoperative adjuvant chemotherapy. Sixty

postoperative chemotherapy patients were randomly divided into 2 groups. The 5-HT receptor inhibitor was applied in one group and large quantity of Stove subsoil decoction was applied in the other group. The curative effect of preventing acute vomiting was similar between 2 groups. But Stove subsoil was better for delayed vomiting, anorexia and diarrhea caused by chemotherapy compared to 5-HT receptor inhibitor (Dang *et al.*, 2012).

Wuwei decoction: Wuwei Decoction was made from *Astragalus membranaceus* (huangqi), *Panax ginseng* (renshen), *acanthopanax root* (ciwujia), *Hedyotis diffusa* (baihuasheshecao), and Chinese blister beetle (banmao). One hundred and fourteen NSCLC patients with postoperative adjuvant chemotherapy were randomly divided into test group and control group. Patients in test group used gemcitabine plus cisplatin program plus Wuwei decoction. The 1 year recurrence rate and 3 year survival rate in 2 groups after treatment had no significant difference. The QoL in test group was obviously better than that in control group; toxicity in test group was significantly lower than that in control group. The results suggested that Wuwei Decoction combined with gemcitabine-cisplatin chemotherapy could effectively improve life quality and reduce toxicity in lung cancer patients (Zhang *et al.*, 2013).

CONCLUSION

Above-mentioned and other evidences demonstrated that a statistically significant increase in survival for those who used various TCM decoction, injection and granules plus chemotherapy compared to those who used chemotherapy alone. They also reduced side effects of conventional chemotherapy and improved the patients' QoL. Therefore, confirmation with large, quality, and rigorously controlled studies is warranted. Further well-designed RCTs of TCM with conventional chemotherapy in cancer patients are needed to provide definitive scientific evidence to determine the optimal doses, duration and timing of their interventions that will modulate cancer patients' immunologic function, reduced tumor burden, improve QoL and prolong survival while minimize the side effects (such as anorexia, fatigue, nausea and vomiting) of major conventional treatment.

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