Traditional Chinese Medicine (TCM) in the Management of Breast and Gynaecological Cancer

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Introduction

Cancer (malignant tumour, neoplasm) is a group of diseases characterized by uncontrolled growth and spread of abnormal cells. Cancer can arise in many sites of the body and is named accordingly after its organ of origin. Breast cancer is mainly diagnosed in women and it is by far the most common female cancer, accounting for around 17% of female deaths from cancer in the UK. Gynaecological cancers, including cancers of the cervix, endometrium, ovary, vagina, vulva and, rarely, the fallopian tube, are the fourth most common form of cancer among women.

Many patients with cancer experience pain, anxiety, and mood disturbances. Despite developments in surgery, chemotherapy, radiation therapy and hormonal therapy and novel immunological and biologically targeted therapies, there are limitations to their benefits in cancer treatment, especially where the disease is advanced. The three conventional treatment modalities (surgery, chemotherapy and radiation therapy) often produce side effects, and the severe side effects caused by chemotherapy often lead to dose reductions or even early discontinuation of the treatment. Furthermore, the side effects often harm a woman's sense of self-esteem, sexuality, and ultimately affect a woman's quality of life. Relief of cancer-related symptoms is essential in the supportive and palliative care of cancer patients. Complementary therapies such as acupuncture and herbal medicine can help when conventional treatment does not bring satisfactory relief or causes undesirable side effects. Many of these therapies are natural, holistic, less intensive and cost effective. They have become more popular over the last decade.

Treatment of breast and gynaecological cancer with traditional Chinese medicine — scientific research and clinical studies

Traditional Chinese medicine (TCM) is an ancient form of medicine founded on thousands of years of experience. TCM therapies mainly include acupuncture / moxibustion and herbal medicine. The management of cancer with TCM began more than two thousand years ago. There have been thousands of case reports showing the benefits of TCM treatment in patients with cancer including gynaecological and breast cancer. Many modern clinical and experimental research studies have further demonstrated the beneficial effects of TCM treatment in cancer care.

Acupuncture

Acupuncture has been recommended by several medical professional bodies, including the American Cancer Society (ACS) for the treatment of cancer and cancer treatment-related symptoms. Pain, nausea, vomiting, breathlessness, vasomotor symptoms and limb

edema have all been found to respond to acupuncture treatment. Acupuncture has also demonstrated immunomodulatory effects as well as alleviating patient's stress through relief of symptoms.

Several randomized clinical trials have shown that acupuncture stimulation effectively relieves nausea and vomiting in cancer patients and can serve as an adjunct to standard anti-emetic medication (Dundee JW et al. 1987; Shen J et al. 1997 and 2000; McMillan C et al. 1991; and Pearl ML et al. 1999)**.** These findings are consistent with a larger body of data supporting the efficacy of various methods of acupuncture stimulation in the control of postoperative (including scheduled gynaecological and breast surgery) nausea and vomiting (Vickers AJ 1996; Al-Sadi M et al. 1997; and Streiberger K et al. 2004). Hamza MA et al. (1999) studied the effects of acupuncture stimulation on the postoperative opioid analgesic requirement and recovery. One hundred women undergoing major gynecological procedures with a standardized general anaesthetic technique were enrolled in the study and randomly assigned to treatment or control groups. In the acupuncture treatment group, the duration of patient-controlled analgesia therapy as well as the incidence of nausea, dizziness, and itching were significantly reduced compared with the control group. They concluded that acupuncture treatment decreased postoperative opioid analgesic requirements and opioid-related side effects when utilized as an adjunct to patient-controlled analgesia after lower abdominal surgery. At the National Institutes of Health (NIH) Consensus Conference in 1998 it was concluded that clear evidence supports the efficacy of acupuncture in the control of post-operative and chemotherapy-related nausea and vomiting (NIH 1998). It is certainly reasonable to accept the use of acupuncture in conjunction with standard anti-emetics to control post-operative and chemotherapy-related nausea and vomiting.

Acupuncture has been shown to provide effective relief when conventional measures fail to control chronic pain resulting from underlying disease or from conventional treatments (surgery, chemotherapy or radiation therapy) (Singh CV 1978; Mann F et al. 1973; Filshie J and Redman D 1985; Filshie J 1988; and Alimi D et al. 2000). A study by He JP, et al. (1999) found a significant relief of post-operative pain and improvement of arm movement with acupuncture treatment in 80 mammary cancer patients after ablation and axillary lymphadenectomy. Acupuncture has also been shown to be effective for chemotherapy-induced leukopenia, post-chemotherapy fatigue, radiation therapy-induced xerostomia, insomnia, and anxiety (Lu W 2005 and Vickers AJ 2004). The effectiveness of acupuncture and moxibustion treatment for lymphedema following intrapelvic lymph node dissection for malignant gynecologic tumours was studied. Twenty four patients were recruited, 12 of them started acupuncture and moxibustion after the occurrence of lymphedema and the other 12 were treated as soon as possible after surgery. A successful treatment or prevention of postoperative lymphedema in the lower extremities was reported in both groups (Kanakura Y et al. 2002).

The immunomodulatory effect of acupuncture has also been studied (Wu B et al. 1994 1995; Liu LJ et al. 1995; and Joos S 2000). The joint study conducted by researchers and medical doctors in China showed that acupuncture can strengthen and regulate the immunity of cancer patients, and significantly lessen the side-effects of chemotherapy

and radiation therapy. Moxibustion on acupuncture points can significantly increase the white blood counts of the patients with late stage cancer. Lymphocyte subgroups CD3+ and CD4+ increased significantly in patients after acupuncture treatment, accompanied by decreased level of interleukin-6 and interleukin-10 and increased level of interleukin-8. Interleukin-2. Natural killer cells were also found increased in cancer patients after acupuncture treatment. The lymphocyte proliferation rate increased after acupuncture treatment. These findings together indicate that acupuncture has immunomodulatory effects, which suggest it can be useful in the treatment of patients with compromised immunity.

Chinese herbal medicine

Since the early 19th century, attempts have been made to understand the property, efficacy and safety of Chinese herbal medicine through scientific research. It was also during this time that most of the drugs used in modern medicine were developed. It is therefore not surprising that most of the scientific research into herbal medicine has attempted to isolate the active ingredients of the herbs and to understand the functions of these ingredients. Chinese herbal medicine has been shown in several clinical studies to relieve symptoms related to cancer or induced by anti-cancer treatments (including chronic pain, nausea, vomiting, fatigue, etc.) and to improve the quality of life of cancer patients (Lin C et al. 1996; Liu F et al. 2003; Zhang XQ et al 1996). The efficacy, safety and side-effects of mistletoe extract (sME), a commonly used Chinese herbal medicine component, was studied in a multi-centric, randomized, prospective clinical trial in China (Piao BK et al. 2004). Two hundred and thirty three patients with breast cancer (n=68), ovarian cancer (n=71) and non-small cell lung cancer (NSCLC, n=94) were enrolled into the study. All patients were treated with standard destructive surgery and complementary sME or placebo in conjunction with chemotherapy according to treatment protocol. Two hundred and twenty-four patients fulfilled the requirements for final analysis. The occurrence of adverse events (due to chemotherapy) was less frequent in the sME group than in the placebo group. The side-effects possibly caused by sME were local inflammatory reactions at subcutaneous injection site and fever, which were self-limiting and did not require medical intervention. Quality of life was significantly improved in sME treated patients as determined by the questionnaires FLIC (Functional Living Index-Cancer), TCMI (Traditional Chinese Medicine Index) and KPI (Karnofsky Performance Index) compared with the placebo group. In a recent paper, Lee TK et al (2005) stated that the water-soluble extract of whole ginseng (a herbal component widely used in traditional Chinese medicine) appears to give a better protection against radiation-induced DNA damage than the isolated ginsenoside fractions. Since free radicals play an important role in radiation-induced damage, the underlying radioprotective mechanism of ginseng could be linked, either directly or indirectly, to its capability of scavenging free radicals. In addition, ginseng's radioprotective potential may due to its immunomodulatory abilities. Ginseng appears to be a promising radioprotector for cancer patients undergoing therapeutic or preventive radiation therapy to attenuate the deleterious effects of the radiation on normal tissues.

The direct inhibitory effects of some herbal medicine on cancer cell growth have been published recently in prestigious medical research journals. Extracts of Angelica sinensis (a traditional Chinese medicine which has been widely prescribed for the treatment of gynecological diseases) showed direct anti-proliferative effect on A549, HT29, DBTRG-05MG and J5 human cancer cells *in vitro*. The induction of G1/S arrest and activation of apoptosis in these cancer cells were also reported (Cheng YL et al. 2004). A special herbal complex (Hoelen, Angelicae radix, Scutellariae radix and Glycyrrhizae radix) was found to induce apoptosis in endocrine-resistant AN3CA cells and adriamycin-resistant MCF7/ADR carcinoma cells. Suppressed telomerase activity was found to contribute to the cellular apoptosis. The results suggested that this herbal complex may be a promising candidate for the treatment of endocrine-resistant gynecologic carcinomas (Lian Z et al. 2003). Tanshinone IIA (a derivative of phenanthrene-quinone isolated from Danshen, a widely used Chinese herbal medicine) has been reported to have antioxidant properties, and cytotoxic activity against multiple human cancer cell lines. The inhibitory effect on human breast cancer cell proliferation was shown *in vitro*. Tumour mass volume reduction was observed in mice treated with Tanshinone. The inhibitory effect was possibly due to upregulation and downregulation of multiple genes involved in cell cycle regulation, cell proliferation, apoptosis, signal transduction, transcriptional regulation, angiogenesis, invasive potential and metastatic potential of cancer cells (Wang X et al. 2005). Several other active components of Chinese herbal medicine such as Indirubin, Ganoderma lucidum (Reishi, Lingzhi), Chlorophyllin (CHL), Herba Scutellaria Barbatae were also reported to have anti-tumour activity both *in vitro* and *in vivo* in a variety of cancers, including breast cancer and ovarian cancer (Nam S et al. 2005; Jiang J et al. 2004; Chiu LC et al. 2003; Powell CB et al. 2003; and Campbell MJ et al 2002).

Conclusions

TCM has a long history in the management of cancer (including breast and gynaecological cancer) patients. Although its primary basis rests on empirical evidence as well as case studies, more modern experimental and clinical researches support the therapeutic modalities in cancer. TCM aims at: relieving symptoms (chronic pain, constipation, bloating, depression and anxiety, etc.), minimizing side effects caused by surgery, chemotherapy and radiation therapy (nausea, vomiting, fatigue, diarrhoea and lymphedema, etc.), improving the immune system, improving sexual function, restoring health, and most importantly, improving patients' quality of life.

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