

# Limiting Chemotherapy Side Effects by Using Moxa

## Abstracts of key publications

Listed below are a number of key publications that have informed our study. They are listed with short summaries describing their contents (called abstracts).

In some cases, the full papers are easily available. In these cases, the link to their webpage is included.

### Key papers

**Staebler F. The daily use of moxibustion to treat chemotherapy-induced bone marrow depression - a practical evaluation based on 20 years of clinical experience. *Journal of Chinese Medicine* 2009;90:65-75.**

#### Abstract

Acupuncture and moxibustion, although not potent enough to act as first line cancer treatments, are powerful tools to support conventional cancer therapy, including surgery, chemotherapy and radiotherapy. In the experience of the author, they can render these interventions better tolerated by patients and lead to more successful treatment outcomes. In particular, they play a significant role in alleviating, and in some cases preventing, the side effects of chemotherapy. This paper focuses on a treatment protocol developed by the author, in which patients and their helpers are taught how to use daily moxibustion at home during chemotherapy. Moxa is used at the acupuncture points Geshu BL-17, Ganshu BL-18 and Pishu BL-20 in order to prevent leukopenia, the dropping of the white blood cell and neutrophil counts (also known as neutropenia). This treatment also helps to prevent anaemia and thrombocytopenia (a drop in the platelet count). The four terms in italics above are also known as pancytopenia, or bone marrow depression. This paper discusses the rationale for using this regimen, and whether it is contraindicated to apply moxibustion during chemotherapy. It also explores some of the technical issues to consider when teaching patients and their helpers how to use moxibustion at home. The article ends with a few selected case histories.

**Davies C. Using a daily home-support moxibustion protocol on St 36 Zu San Li during chemotherapy: a case history. *European Journal of Oriental Medicine* 2013;7(4):34-39.**

#### Abstract

A daily home-use moxibustion (moxa) protocol for nourishing the immune system during chemotherapy, first described by Dr Friedrich Staebler (Staebler, 2006), allows a patient to participate positively in his or her immune support during the entire period. The protocol requires the patient to have a helper to apply moxa daily on back *shu* points. This paper discusses a variation on the existing protocol, which allows a patient without available help to be self-supporting on this.

**Choi T-Y, Lee MS, Ernst E. Moxibustion for the treatment of chemotherapy-induced leukopenia: a systematic review of randomized clinical trials. *Supportive Care in Cancer* 2015;23(6):1819-1826.**

#### Abstract

##### PURPOSE:

The purpose of this study is to assess the efficacy of moxibustion as a treatment of chemotherapy-induced leukopenia.

##### METHODS:

Twelve databases were searched from their inception through June 2014, without a language restriction. Randomized clinical trials (RCTs) were included if moxibustion was used as the sole treatment or as a part of a combination therapy with conventional drugs for leukopenia induced by chemotherapy. Cochrane criteria were used to assess the risk of bias.

## RESULTS:

Six RCTs with a total of 681 patients met our inclusion criteria. All of the included RCTs were associated with a high risk of bias. The trials included patients with various types of cancer receiving ongoing chemotherapy or after chemotherapy. The results of two RCTs suggested the effectiveness of moxibustion combined with chemotherapy vs. chemotherapy alone. In four RCTs, moxibustion was more effective than conventional drug therapy. Six RCTs showed that moxibustion was more effective than various types of control interventions in increasing white blood cell counts.

## CONCLUSIONS:

There is low level of evidence based on these six trials that demonstrates the superiority of moxibustion over drug therapies in the treatment of chemotherapy-induced leukopenia. However, the number of trials, the total sample size, and the methodological quality are too low to draw firm conclusions. Future RCTs appear to be warranted.

**Lu W, Matulonis U, Doherty-Gilman A, et al. Acupuncture for chemotherapy-induced neutropenia in patients with gynecologic malignancies: a pilot randomized, sham-controlled clinical trial *Journal of Alternative and Complementary Medicine* 2009;15(7):745-753.**

## Abstract

### Objectives

The objective of this study was to investigate the effect of acupuncture administered during myelosuppressive chemotherapy on white blood cell (WBC) count and absolute neutrophil count (ANC) in patients with ovarian cancer.

### Design

This study is a pilot, randomized, sham-controlled clinical trial. Patients received active acupuncture versus sham acupuncture while undergoing chemotherapy. A standardized acupuncture protocol was employed with manual and electrostimulation. The frequency of treatment was 2–3 times per week for a total of 10 sessions, starting 1 week before the second cycle of chemotherapy.

### Setting

The setting was two outpatient academic centers for patients with cancer.

### Subjects

Twenty-one (21) newly diagnosed and recurrent ovarian cancer patients were the subjects.

### Outcome measures

WBC count, ANC, and plasma granulocyte colony-stimulating factor (G-CSF) were assessed weekly.

### Results

The median leukocyte value in the acupuncture arm at the first day of the third cycle of chemotherapy was significantly higher than in the control arm after adjusting for baseline value (8600 cells/ $\mu$ L, range: 4800–12,000 versus 4400 cell/ $\mu$ L, range: 2300–10,000) ( $p = 0.046$ ). The incidence of grade 2–4 leukopenia was less in the acupuncture arm than in the sham arm (30% versus 90%;  $p = 0.02$ ). However, the median leukocyte nadir, neutrophil nadir, and recovering ANC were all higher but not statistically significantly different ( $p = 0.116$ – $0.16$ ), after adjusting for baseline differences. There were no statistically significant differences in plasma G-CSF between the two groups.

### Conclusions

We observed clinically relevant trends of higher WBC values during one cycle of chemotherapy in patients with ovarian cancer, which suggests a potential myeloprotective effect of acupuncture. A larger trial is warranted to more definitively determine the efficacy of acupuncture on clinically important outcomes of chemotherapy-induced neutropenia.

**Pais I, Correia N, Pimentel I, et al. Effects of acupuncture on leucopenia, neutropenia, NK, and B cells in cancer patients: a randomized pilot study. *Evidence-Based Complementary and Alternative Medicine* 2014.**

Full publication is available at <http://www.hindawi.com/journals/ecam/2014/217397/>

## Abstract

Chemotherapy is one of most significant therapeutic approaches to cancer. Immune system functional state is considered a major prognostic and predictive impact on the success of chemotherapy and it has an important role on patients' psychoemotional state and quality of life. In Chinese medicine,

chemotherapy is understood as “toxic cold” that may induce a progressive hypofunctional state of immune system, thus compromising the fast recovery of immunity during chemotherapy. In this study, we performed a standardized acupuncture and moxibustion protocol to enhance immunity in cancer patients undergoing chemotherapy and to assess if the improvement of immunity status correlates with a better psychoemotional state and quality of life.

**Bovey M. Acupuncture for chemotherapy-induced neutropenia and leukopenia: a review of the literature [online]. 2009.**

Full paper available at:

<http://www.davidkelsey.co.uk/acupuncture-supporting-cancer-patients.html>

**Lee MS, Choi T-Y, Park J-E, et al. Moxibustion for cancer care: a systematic review. BMC Cancer 2010;10(130).**

Full paper available at: <http://www.biomedcentral.com/1471-2407/10/130>

## Abstract

### Background

Moxibustion is a traditional Chinese method that uses the heat generated by burning herbal preparations containing *Artemisia vulgaris* to stimulate acupuncture points. Considering moxibustion is closely related to acupuncture, it seems pertinent to evaluate the effectiveness of moxibustion as a treatment of symptoms of cancer. The objective of this review was to systematically assess the effectiveness of moxibustion for supportive cancer care.

### Methods

We searched the literature using 11 databases from their inceptions to February 2010, without language restrictions. We included randomised clinical trials (RCTs) in which moxibustion was employed as an adjuvant treatment for conventional medicine in patients with any type of cancer. The selection of studies, data extraction, and validations were performed independently by two reviewers.

### Results

Five RCTs compared the effects of moxibustion with conventional therapy. Four RCTs failed to show favourable effects of moxibustion for response rate compared with chemotherapy (n = 229, RR, 1.04, 95% CI 0.94 to 1.15, P = 0.43). Two RCTs assessed the occurrence of side effects of chemotherapy and showed favourable effects of moxibustion. A meta-analysis showed significant less frequency of nausea and vomiting from chemotherapy for moxibustion group (n = 80, RR, 0.38, 95% CIs 0.22 to 0.65, P = 0.0005, heterogeneity:  $\chi^2 = 0.18$ , P = 0.67,  $I^2 = 0\%$ ).

### Conclusion

The evidence is limited to suggest moxibustion is an effective supportive cancer care in nausea and vomiting. However, all studies have a high risk of bias so effectively there is not enough evidence to draw any conclusion. Further research is required to investigate whether there are specific benefits of moxibustion for supportive cancer care.

**Kim S-Y, Chae Y, KLee SM, et al. The effectiveness of moxibustion: an overview during 10 years. Evidence-Based Complementary and Alternative Medicine 2011;2001(Article ID 306515).**

Full paper available at <http://www.hindawi.com/journals/ecam/2011/306515/>

## Abstract

Moxibustion has been used to treat various types of disease. However, there is still insufficient evidence regarding its effectiveness. This study was performed to summarize and evaluate the effectiveness of moxibustion. A search was performed for all randomized controlled trials in PubMed between January 1998 and July 2008 with no language restriction. The results yielded 47 trials in which six moxibustion types were applied to 36 diseases ranging from breech presentation to digestive disorders. Moxibustion was compared to three types of control group: general care, Oriental medical therapies or waiting list. Moxibustion was superior to the control in 14 out of 54 control groups in 46 studies. There were no significant differences among groups in 7 studies, and the outcome direction was not determined in 33 studies. Seven studies were included in a meta-analysis.

Moxibustion was more effective than medication in two ulcerative colitis studies (relative risk (95% CI), 2.20 (1.37, 3.52),  $P = .001$ ,  $I^2 = 0\%$ ). Overall, our results did not support the effectiveness of moxibustion in specific diseases due to the limited number and low quality of the studies and inadequate use of controls. In order to provide appropriate evidence regarding the effectiveness of moxibustion, more rigorous clinical trials using appropriate controls are warranted.

**Park J-E, Lee S-S, Lee MS, et al. Adverse events of moxibustion: a systematic review. *Complementary Therapies in Medicine* 2010;18(5):215-223.**

## **Abstract**

### **OBJECTIVES:**

The aim of this review was to identify adverse events of moxibustion as reported in the medical literature.

### **METHODS:**

Computerised literature searches were carried out in 14 databases. All articles reporting adverse effects of any type from moxibustion in humans were included, regardless of study design and publication language. The related journals and references in all located articles were manually searched for further relevant articles. Data were extracted and evaluated according to predefined criteria by three independent reviewers.

### **RESULTS:**

Adverse events related to moxibustion treatment were reported in 4 randomised clinical trials, 1 controlled clinical trial, 2 uncontrolled observational studies, 13 case reports, and 1 prospective study. The most common effects identified in this review were allergic reactions, burns, and infections such as cellulitis and hepatitis C. Allergic reactions were reported in six case reports (four case reports related to infections and two related to burns). The other articles were case reports of xerophthalmia, xeroderma, hyperpigmented macules, ptosis and eversion of the eyelids. In clinical trials, various adverse events such as rubefaction, blistering, itching sensations, discomfort due to smoke, general fatigue, stomach upsets, flare-ups, headaches, and burns were reported. Tenderness and pressure in the epigastric region or in one of the hypochondriac regions, unpleasant odour with or without nausea and throat problems, abdominal pain, premature birth, premature rupture of the membrane and bleeding due to excess pressure on the anterior placenta were reported in pregnant women.

### **CONCLUSION:**

Moxibustion is not entirely risk free, as it has several kinds of potential adverse events such as allergy, burn and infection. Currently, the incidence of such events is not known. In the interest of patient safety, sufficiently large prospective studies should be considered to clarify this issue.

## **Other papers**

**Johnston M, Sanchez E, Vujanovic NL, et al. Acupuncture may stimulate anticancer immunity via activation of natural killer cells *Evidence-Based Complementary and Alternative Medicine* 2011.**

Full publication is available at <http://www.hindawi.com/journals/ecam/2011/481625/>

## **Abstract**

This article presents the hypothesis that acupuncture enhances anticancer immune functions by stimulating natural killer (NK) cells. It provides background information on acupuncture, summarizes the current scientific understanding of the mechanisms through which NK cells act to eliminate cancer cells, and reviews evidence that acupuncture is associated with increases in NK cell quantity and function in both animals and humans. The key contribution of this article involves the use of cellular immunology and molecular biological theory to interpret and synthesize evidence from disparate animal and human studies in formulating the 'acupuncture immuno-enhancement hypothesis': clinicians may use acupuncture to promote the induction and secretion of NK-cell activating cytokines that engage specific NK cell receptors that endogenously enhance anticancer immune function.

**Yim Y-K, Lee H, Hong K-E, et al. Electro-Acupuncture at Acupoint ST36 Reduces Inflammation and Regulates Immune Activity in Collagen-Induced Arthritic Mice. *Evidence-Based Complementary and Alternative Medicine* 2007;4(1):51-57.**

Full publication available at <http://www.hindawi.com/journals/ecam/2007/521063/abs/>

#### **Abstract**

This study aimed to investigate the anti-inflammatory, anti-arthritic and immuno-regulatory effects of electro-acupuncture (EA) at ST36 on Collagen-induced arthritis (CIA) in mice. Male DBA/1J mice were divided into five groups: Normal, Control, NR (needle retention), EAI and EAll. All mice except those in the normal group were immunized with Collagen II for arthritis induction. Acupuncture needles were inserted into mice ST36 and electrical currents at a frequency of 2 Hz in a continuous rectangular wave form were conducted through the needles for 15 min, 3 times a week. EA treatments were administered for 5 weeks in the EAI group and for 9 weeks in the EAll group. The mice in the NR group were acupunctured in the same manner as the EA groups and the needles were retained for 15 min without electrical stimulation. CIA incidence analysis, ELISA, histological analysis and FACS analysis were performed to evaluate the effect of EA on CIA. EA at ST36 significantly reduced CIA incidence, IL-6, TNF- $\alpha$ , INF- $\gamma$ , collagen II antibody, IgG and IgM levels in CIA mice serum and prevented knee joint destruction. EA at ST36 also reduced CD69+/CD3e+ cells and CD11a+/CD19+ cells in CIA mice lymph nodes, and CD11b+/Gr1+ cells in CIA mice knee joints. The ratios of CD3e+ cells to CD19+ cells, and CD8+ cells to CD4+ cells were maintained closer to the normal range in the EA groups as compared with the control group or the NR group. EAll was more effective than EAI throughout all the measurements. The NR was effective as well, though less effective than EA. EA at ST36 may have an anti-inflammatory, anti-arthritic and immuno-regulatory effects on CIA in mice. The effectiveness is stronger when EA starts earlier and is applied longer. Needle retention without electrical stimulation may be effective on CIA as well, however less effective than EA. Electrical stimulation and acupoint ST36 may have synergistic effects on CIA.

**Peng L, Liu M, Chang X, et al. Effects of pre-moxibustion at Zusanli (ST36) on heat shock protein 70 expression in rats with gastric mucosal lesions after neurotomy. *Neural Regeneration Research* 2012;7(30):2370-2376.**

#### **Abstract**

Studies have shown that pre-moxibustion protects the gastric mucosa by up-regulating the expression of heat shock protein 70. However, the signaling pathway underlying this effect remains unclear. Rats were intragastrically administered absolute alcohol, causing obvious lesion of the gastric mucosa. Following pre-moxibustion at *Zusanli* (ST36) for 8 days, the ulcer index decreased to different degrees. The results of an enzyme linked immunosorbent assay and western blotting showed significant upregulation of heat shock protein 70 expression in the gastric mucosa and serum. None out of transection of the spinal cord, damage to the nucleus of the solitary tract, neurotomy of the vagal nerve and neurotomy of the common peroneal nerve affected the decrease in ulcer index or the increase in heat shock protein 70 expression in serum after pre-moxibustion at *Zusanli*, and heat shock protein 70 expression was obviously decreased in the gastric mucosa. These findings suggest that pre-moxibustion at *Zusanli* can protect the gastric mucosa against lesioning, and that the mechanism underlying this effect involves its induction of heat shock protein 70 expression. Neural pathways participate in the regulatory effects of moxibustion on heat shock protein 70 expression in the gastric mucosa.

**Zhang H, Lin Z, Cheung F, et al. Moxibustion for alleviating side effects of chemotherapy or radiotherapy in cancer patients (protocol). *Cochrane Database of Systematic Reviews* 2013;Issue 6(ART No: CD010559).**

Full paper available at:

<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010559/epdf>