

# Effects of Acupoint Application Therapy on Quality of Life of Patients with Cancer-Related Fatigue During Chemotherapy for Lymphoma

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## Abstract

**Objective:** To evaluate the effects of acupoint application therapy on the quality of life of patients with cancer-related fatigue (CRF) during chemotherapy for lymphoma.

**Methods:** Lymphoma patients treated in Department of Hematology, Jiangsu Cancer Hospital from September 2018 to February 2019 were selected through convenience sampling. A total of 96 patients who had mild and severer CRF rated by the Piper fatigue scale during chemotherapy were divided into control group (n=49) and experimental group (n=46) using a random number table. The control group was given conventional nursing during chemotherapy, while the experimental group received acupoint application therapy with Chinese materia medica applied to Shenque, Guanyuan and Zusanli (4-6 h/d, with 5 d as a course of treatment). After treatment, the quality of life, physical function status, performance status, 120 h response rate and incidence rate of adverse reactions were compared between the two groups.

**Results:** The total quality-of-life score, KPS score and 120 h therapeutic index were higher in experimental group than those in control group after treatment (P<0.05). No adverse reactions occurred during treatment in control group, while 2 (4.35%) patients in experimental group suffered from skin-mucous membrane reaction at Shenque acupoint due to medication time prolonged by themselves, which was cured after drug withdrawal for 1 d.

**Conclusion:** Acupoint application therapy with Chinese materia medica has obvious efficacy on CRF during chemotherapy for lymphoma and can efficiently improve the quality of life of patients.

**Keywords:** lymphoma' chemotherapy; cancer-related fatigue; quality of life.

## 1. Introduction

Malignant tumor, one of the life-threatening diseases, has rising morbidity and mortality rates, and its morbidity rate increases at an annual rate of 3-5% in China.

The incidence rate of lymphoma, a kind of tumor with fairly high malignancy and mortality rate, is rising at a rate of 6% every year as well, and chemotherapy is currently considered as the major treatment protocol for this disease [1]. Cancer-related fatigue (CRF) refers to the subjective feeling of patients that occurs frequently when they experience tumor or receive tumor treatment, with low energy, low spirits and loss of interest as the main clinical manifestations. Such fatigue cannot be relieved through rest and sleeping, seriously affecting the physiological, psychological and social functions of patients and reducing their quality of life [2,3]. At present, there is no western medicine for CRF in clinic, and only symptomatic treatment

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should be conducted according to patients' clinical manifestations, but its efficacy lasts for a short time, the recurrence rate is high, and great toxic and side effects of drugs are induced, thus usually aggravating the CRF in patients. It is argued in traditional Chinese medicine that CRF belongs to "consumptive diseases", which is related to impairment of primordial qi due to tumor ingrowth, depletion of primordial qi due to surgery and chemoradiotherapy for eliminating pathogen, depletion and impairment of qi and blood due to emotional disorders and impairment of qi and blood due to sleep disorders. In this study, based on the pathogenesis of "deficiency of vital qi" of CRF [3] and the treatment principle of "benefiting the vital qi", the CRF emerging during chemotherapy was treated by means of acupoint application therapy, thereby alleviating the discomfort and improving the quality of life of patients. The results of this study are expected to provide references for future clinical treatment.

## 2 Materials and Methods

### 2.1 Clinical data

Lymphoma patients treated in Department of Hematology, Jiangsu Cancer Hospital from September 2018 to February 2019 were enrolled, and 96 patients who had mild and severer CRF rated by the Piper fatigue scale during chemotherapy were randomly grouped. There were 54 males and 41 females aged ( $43.17 \pm 19.24$ ) years old on average. Inclusion criteria: (1) Patients who had good general

conditions and a Karnofsky performance status (KPS) score  $\geq 60$  points and were willing to receive the treatment protocol in this study; (2) those definitely diagnosed as malignant lymphoma by clinical symptoms, imaging and pathology and not complicated with other malignant tumors; (3) those who were undergoing CHOP and R-CHOP chemotherapy regimens; (4) those aged  $\geq 18$  years old; (5) those with a life expectancy of more than 3 months; (6) those who had cognitive ability, could complete relevant questionnaires independently and signed the informed consent. Exclusion criteria: (1) Patients with skin lesions; (2) those allergic to Chinese herbal formulas; (3) those with nerve compression syndrome and disappearance of physiological reflex of both lower extremities due to brain metastasis and extremity metastasis; (4) those with diseases in such organs as the heart, brain, liver and kidney; (5) those who suffered from depression, schizophrenia or other mental diseases or were taking medicines; (6) those who were unaware of their own disease. All the selected patients were assigned into control group ( $n=49$ ) and experimental group ( $n=46$ ) using a random number table, and the general conditions, including gender, occupation, educational level, religious belief and fatigue score based on Ann Arbor stage, before treatment showed no statistical differences between the two groups ( $P>0.05$ ). The fatigue scores based on the general data of the two groups are listed in Table 1.

Table 1. Fatigue scores based on general data of two groups ( $\bar{x} \pm s$ , point)

Item			Experimental group	Control group	Statistics	P
Gender	Fatigue score	Male	5.73 $\pm$ 1.03	6.14 $\pm$ 0.78	1.614 <sup>a</sup>	0.113
		Female	6.24 $\pm$ 1.75	6.71 $\pm$ 1.18	0.991 <sup>a</sup>	0.328
	Case No.	Male	24	30	0.792 <sup>b</sup>	0.374
		Female	22	19		
Occupation	Fatigue score	With jobs	7.24 $\pm$ 1.95	8.07 $\pm$ 1.66	1.053 <sup>a</sup>	0.306
		Without jobs	6.26 $\pm$ 2.12	2.12 $\pm$ 1.43	1.747 <sup>a</sup>	0.087
	Case No.	With jobs	19	22	0.125 <sup>b</sup>	0.734
		Without jobs	27	27		
Educational level	Fatigue score	Primary school	5.88 $\pm$ 2.41	5.16 $\pm$ 1.96	0.559 <sup>a</sup>	0.589
		Junior high school	6.48 $\pm$ 1.49	6.18 $\pm$ 0.96	0.482 <sup>a</sup>	0.589
		Senior high school	6.76 $\pm$ 2.24	7.04 $\pm$ 1.66	0.358 <sup>a</sup>	0.723
		Above senior high school	7.42 $\pm$ 1.99	7.88 $\pm$ 1.74	0.834 <sup>a</sup>	0.588
	Case No.	Primary school	4	8	3.602 <sup>b</sup>	0.308
		Junior high school	15	19		
Senior high school		18	11			

		Above senior high school	9	11		
Ann Arbor stage	Fatigue score	I	5.62±2.77	6.82±1.95	0.728 <sup>a</sup>	0.494
		II	5.82±2.54	5.62±2.05	0.272 <sup>a</sup>	0.787
		III	7.32±1.86	7.78±1.84	0.627 <sup>a</sup>	0.537
		IV	7.79±2.12	7.04±2.58	0.731 <sup>a</sup>	0.474
	Case No.	I	3	5	1.169 <sup>b</sup>	0.760
		II	21	19		
		III	11	15		
		IV	11	10		

<sup>a</sup>: t value; <sup>b</sup>:  $\chi^2$  value.

## 2.2 Methods

In control group, the patients were given conventional nursing of lymphoma during chemotherapy. The patients in experimental group were treated with acupoint application of traditional Chinese medicine on the basis of conventional nursing. 1) In terms of Chinese herbal formula and preparation, 2 portions of *Radix Codonopsis*, 5 portions of *Astragalus membranaceus*, 2 portions of *Ophiopogon japonicus*, 2 portions of *Radix Paeoniae Alba*, 2 portions of *Poria Cocos*, 2 portions of *Cornus officinalis*, 5 portions of *Dioscorea opposita Thunb*, 2 portions of *Atractylodes Macrocephala Koidz*, 1 portion of *Ramulus Cinnamomi* and 1 portion of glycyrrhiza were ground into fine powders with a particle size of 100-150 mesh using an ultra-fine grinder, which was prepared into a paste with 4 portions of maltose and then made into pills with a diameter of 1 cm. 2) Shenque, Guanyuan and bilateral Zusanli acupoints were selected. 3) As for the usage, every acupoint was first massaged for 1 min, then the site of acupoint application was wiped by an alcohol pad, and the prepared pill was placed at the acupoint and covered with a transparent film. The patch was applied for 4-6 h for 5 consecutive days. The quality of life, physical function status, 120 h therapeutic index rate and incidence rate of adverse reactions were compared at 7 d after medication between the two groups.

## 2.3 Evaluation criteria

(1) According to the scores of the Piper fatigue scale before and after intervention, the 120 h therapeutic index was calculated as follows: 120 h therapeutic index = (score before treatment - score after treatment)/score before treatment ×100%, including grade I: clinical remission [The symptoms and signs are completely ameliorated after medication (therapeutic index ≥95%), grade II: markedly effective [The symptoms and signs are remarkably improved after medication (70%≤ therapeutic index <95%), grade III: effective [The

symptoms and signs are certainly mitigated after medication (30%≤ therapeutic index <70%)] and grade IV: ineffective [The symptoms and signs are not obviously relieved or aggravated after medication (therapeutic index <30%)]. (2) The quality of life was evaluated using the EORTC Core Quality-of-Life Questionnaire for cancer patients containing 30 items in total. The function items consist of physical functioning (PF), role functioning (RF), emotional functioning (EF), cognitive functioning (CF) and social functioning (SF), and the symptom items include fatigue, nausea and vomiting, pain, respiration disorder, insomnia, appetite, diarrhea and general health status. The 4-point Likert scoring method was adopted, and the score was 0-100 points in total. Higher scores of function dimensions and general health status indicate better functions and health status, while a higher score of symptom dimensions suggests severer symptoms. (3) The health status was evaluated using the KPS that is applied to assess the daily self-care ability, motility and dependence degree of medical care of cancer patients. The scale has been widely used for the functional status evaluation of cancer patients so far, with a total score of 100 points and 10 grades (10 points for each grade). A higher score means better health status and higher tolerance to side effects of treatment. On the contrary, a low score indicates a poor health status, and many efficacious antitumor therapies cannot be implemented when the score is lower than 60 points. The patients in both groups were scored using the KPS scoring standards as indicators before and after treatment, and the scores were classified as increased (the score is raised by ≥10 points after treatment compared with that before treatment), decreased (the score is reduced by ≥10 points) and stable (the score is raised or reduced by <10 points). (4) The adverse drug reactions were evaluated according to the National Cancer Institute Common Terminology Criteria for Adverse Events-

V4.0 [8], and the incidence rate of adverse reactions were compared between the two groups.

#### 2.4 Statistical analysis

All data were statistically analyzed by SPSS 25.0 software. The quantitative data were expressed as ( $\bar{x} \pm s$ ), and intergroup comparisons were performed with the t test. The numerical data were represented as percentage and subjected to the two-

independent sample  $\chi^2$  test.  $P < 0.05$  was considered statistically significant.

### 3. RESULTS

#### 3.1 120 h therapeutic index after treatment

The 120 h therapeutic indices of the two groups after treatment are shown in Table 2.

**Table 2.** 120 h therapeutic index after treatment (%)

Group	Case No.	Clinically remitted (index $\geq 95\%$ )	Markedly effective (70% $\leq$ index $< 95\%$ )	Effective (30% $\leq$ index $< 70\%$ )	Ineffective (index $< 30\%$ )	$\chi^2$	P
Experimental	46	33 (71.74)	7 (6.52)	3 (6.52)	3 (6.52)	20.65	0.00
Control	49	14 (28.57)	9 (18.37)	9 (18.37)	17 (34.69)	7	0

#### 3.2 KPS score 7 days after treatment

The KPS scores of the two groups 7 days after treatment are summarized in Table 3.

**Table 3.** KPS score 7 days after treatment [case (%)]

Group	Case No.	Increased	Stable	Decreased	Clinical benefit rate
Experimental	46	32 (69.57)	11 (23.91)	3 (6.52)	43 (93.48)
Control	49	17 (34.69)	18 (36.73)	14 (28.57)	35 (71.43)
$\chi^2$					7.81
P					0.005

#### 3.3 QLQ-C30 score 7 days after treatment

The QLQ-C30 scores of the two groups 7 days after treatment are exhibited in Table 4.

**Table 4.** QLQ-C30 score 7 days after treatment

QLQ-C30	Item	Experimental group (n=46)	Control group (n=49)	t	P
Functional scale	PF	67.67 $\pm$ 17.06	54.42 $\pm$ 21.39	3.324	0.001
	RF	47.51 $\pm$ 7.06	39.42 $\pm$ 6.95	5.627	0.000
	EF	70.12 $\pm$ 9.95	65.61 $\pm$ 8.11	2.428	0.017
	CF	72.42 $\pm$ 12.96	66.81 $\pm$ 8.91	2.471	0.015
	SF	49.48 $\pm$ 8.54	42.43 $\pm$ 9.98	3.876	0.000
General health scale		66.24 $\pm$ 13.78	58.53 $\pm$ 11.23	2.997	0.004
Symptom scale	Fatigue	32.18 $\pm$ 17.08	57.15 $\pm$ 12.46	8.176	0.000
	Nausea and vomiting	25.96 $\pm$ 20.76	34.03 $\pm$ 26.02	1.664	0.100
	Pain	44.43 $\pm$ 9.98	44.18 $\pm$ 8.54	0.131	0.896
	Shortness of breath	26.18 $\pm$ 10.46	34.43 $\pm$ 7.08	4.474	0.000
	Insomnia	29.27 $\pm$ 7.89	28.78 $\pm$ 8.41	0.292	0.770
	Loss of appetite	27.21 $\pm$ 12.81	31.88 $\pm$ 13.86	2.632	0.010
	Constipation	34.43 $\pm$ 9.98	37.18 $\pm$ 8.54	1.446	0.152
	Diarrhea	28.78 $\pm$ 8.41	29.27 $\pm$ 7.08	0.308	0.759
	Low income	49.46 $\pm$ 9.98	50.18 $\pm$ 8.54	0.379	0.706

### 3.4 Drug adverse reactions

The control group received no medication, while 2 (4.35%) patients in experimental group suffered from skin-mucous membrane reaction at Shenque acupoint because of medication time prolonged by themselves, which was cured after drug withdrawal for 1 d.

## 4. DISCUSSION

### 4.1 Theoretical basis of treating CRF with acupoint application therapy

The drugs stimulate local acupoints to dredge the channels and collaterals, regulate qi and blood, reinforce deficiency and reduce excess, regulate the yin and yang of zang-fu viscera, thus balancing human performance, restoring health and reaching an "equilibrium of yin and yang". According to the traditional Chinese medicine nursing based on syndrome differentiation as well as the nature, flavor and meridian tropism of drugs, the acupoints were selected based on syndrome differentiation in the present study: 1) Shenque is a commonly used acupoint for external application of Chinese materia medica, which is located at the umbilicus and belongs to Ren meridian. The Ren meridian is the sea of yin meridians, while the Du meridian is the governor of yang meridians, both of which supplement each other and jointly dominate various meridians. Therefore, there is also a theory of "one source and three branches" about Shenque, where it can circulate the channel-qi into five-zang organs and six-fu organs, limbs and skeletons, five sensory organs and nine orifices as well as skin, flesh, tendon and bone, thereby promoting the movement of qi and blood and regulating the balance between yin and yang of zang-fu viscera. In combination with the theory of "transdermal drug delivery system" in modern medicine, the thin keratoderma around the umbilicus and the abundant blood vessels facilitate the drug permeation and absorption, so Shenque is the main point of application. 2) Guanyuan is capable of dredging the channels and collaterals to treat diseases of pericardium meridian and forearms. The heart dominates blood circulation and vessels, and the pericardium and heart share the same origin and qi flow. The pericardium is the outer membrane of the heart, and collaterals are the passages of qi and blood outside the membrane. The mental diseases caused by pathogens invading pericardium and the disease symptoms induced by qi stagnation in pulse and blood stasis blocking heart collateral can be cured by treating Guanyuan acupoint. Particularly, the adverse rising of lung and

stomach qi induced by emotional disharmony and qi blockage can also be cured through this acupoint. Hence, Guanyuan acupoint was applied with drug plaster prepared by ginger pop for the patients with vomiting in this study. 3) Zusanli, one of the main points of Yangming stomach meridian of foot, is able to harmonize the spleen and stomach, invigorate spleen-stomach and replenish qi, activate channels and collaterals, expel wind and resolve dampness, and strengthen vital qi to eliminate pathogenic factors. It has been verified by modern medical research that stimulating Zusanli acupoint can promote gastrointestinal peristalsis, increase the activity of digestive enzyme, enhance appetite and help with digestion. Moreover, it can improve the cardiac function, regulate cardiac rhythm and raise the levels of erythrocytes, leukocytes, hemochrome and blood glucose. In terms of the endocrine system, Zusanli acupoint has a bidirectional benign regulating effect on the function of pituitary-adrenocortical system, thus increasing the defense ability of the body against diseases. It is well-established in traditional Chinese medicine that chemotherapy-induced hiccup is mostly caused by impairment of vital qi due to a long illness, body deficiency or excessive vomiting. Therefore, the invasion of deficiency-syndrome impairs the middle qi, weakens the spleen and stomach and leads to failure of stomach qi to descend or stomach-yin deficiency and failure of stomach downward propelling, so the adverse rising of stomach qi stimulates the diaphragm to trigger hiccup. Therefore, Zusanli acupoint can benefit the vital qi, nourish yin and relieve hiccup.

### 4.2 Comparison of quality of life 7 days after treatment

(1) There were significant differences in the scores of PF, RF, CF, SF and EF between the two groups, suggesting that experimental group has superior PF to control group. (2) It was shown in the comparison of quality-of-life score between the two groups that the average score in experimental group was 0.29 points lower than that in control group, without a statistical difference. Since this indicator is an overall evaluation index for the own quality of life of patients, the inaccurate score may be attributed to the obscure self-evaluation criteria of patients. (3) Experimental group exhibited higher scores of symptoms such as fatigue, short breath and loss of appetite than control group, while no prominent differences in the scores of pain, nausea and vomiting, insomnia, diarrhea and constipation were observed between the two groups.

#### 4.3 Comparison of 120 h therapeutic indices after treatment

Based on the comparison of the 120 h therapeutic index, the effective rate was raised in experimental group in contrast with that in control group, and the difference was statistically significant between the two groups ( $P < 0.05$ ).

#### 4.4 Comparison of KPS scores 7 days after treatment

According to the comparison of KPS score at 7 d after treatment, experimental group had a higher clinical benefit rate than control group, with a statistical difference ( $P < 0.05$ ).

In conclusion, acupoint application therapy based on the treatment principle of benefiting the vital qi can supplement qi and consolidate vital base, nourish yin and clear heat, and invigorate spleen and emolliate liver, thereby effectively alleviating chemotherapy-induced CRF [11], ameliorating patients' health status and improving the quality of life. The acupoint application therapy with Chinese materia medica is characterized by multiple targets, no trauma, mild side effects, low cost and favorable compliance of patients, providing new ideas for the adjunctive therapy for lymphoma patients during chemotherapy.

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