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The effect of acupuncture on chemotherapy-associated gastrointestinal symptoms in gastric cancer

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ABSTRACT

Background Gastrointestinal (GI) symptoms are the most notable side effects of chemotherapeutic drugs; such symptoms are currently treated with drugs. In the present study, we investigated the effect of acupuncture on GI symptoms induced by chemotherapy in patients with advanced gastric cancer.

Methods A cohort of 56 patients was randomly divided into an experimental group and a control group. All patients received combination chemotherapy with oxaliplatin–paclitaxel. Patients in the experimental group received 30 minutes of acupuncture therapy daily for 2 weeks. The frequency and duration of nausea, vomiting, abdominal pain, and diarrhea, the average days and costs of hospitalization, and quality-of-life scores were compared between the groups.

Results Nausea was sustained for 32 ± 5 minutes and 11 ± 3 minutes daily in the control and experimental groups respectively ($p < 0.05$). On average, vomiting occurred 2 ± 1 times daily in the experimental group and 4 ± 1 times daily in the control group ($p < 0.05$). Abdominal pain persisted for 7 ± 2 minutes and 16 ± 5 minutes daily in the experimental and control groups respectively ($p < 0.05$). On average, diarrhea occurred 1 ± 1 times daily in the experimental group and 3 ± 1 times daily in the control group ($p < 0.05$). The average quality-of-life score was higher in the experimental group than in the control group ($p < 0.05$). No adverse events were observed for the patients receiving acupuncture.

Conclusions Acupuncture, a safe technique, could significantly reduce GI symptoms induced by chemotherapy and enhance quality of life in patients with advanced gastric cancer.

Key Words Acupuncture, gastric cancer, chemotherapy, gastrointestinal symptoms, quality of life

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INTRODUCTION

Gastric cancer is a common gastrointestinal (GI) malignancy, accounting for the 5th-highest incidence of malignant tumours worldwide. Each year, approximately 1 million people are diagnosed with gastric cancer and approximately 700,000 die of the disease[1]. Because of a combination of diet, genetics, and a high prevalence of *Helicobacter pylori*, populations of the countries of East Asia, including China, have a notably high incidence of gastric cancer.

A proportion of patients with advanced gastric cancer do not qualify for surgical treatment because of distant lymph node or organ metastasis, poor systemic condition (severe anemia, low serum albumin), or severe heart or lung disease and therefore can receive only nonsurgical treatments. Interventions using a combination of chemotherapy, gene-targeted therapy, or radiotherapy have been widely applied, effectively prolonging the survival of patients with advanced gastric cancer[2–4]. However, the side effects of chemotherapy can worsen a patient's quality of life, possibly even hindering continuation of treatment and rendering the patient vulnerable to disease progression and death. Common side effects of chemotherapy include bone marrow suppression, GI symptoms (nausea, vomiting, loss of appetite, abdominal bloating, abdominal pain, diarrhea, GI tract bleeding, and so on), hepatic or renal dysfunction, myocardial damage, hand–foot syndrome, and allergies[5–7]. Many

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patients have had underlying mild or severe GI symptoms for a long time because of chronic atrophic gastritis before the onset of gastric cancer—a group in whom chemotherapy exacerbates GI symptoms.

Currently, chemotherapy-related GI symptoms are relieved mostly with medications. For example, 5-hydroxytryptamine inhibitors are used to treat vomiting, and proton pump inhibitors help to prevent and treat upper GI tract hemorrhaging. New approaches to relieve chemotherapy-related GI symptoms for better effectiveness and successful completion of the treatment regimen are therefore of great interest for clinicians.

Acupuncture has a long history within Traditional Chinese Medicine (TCM) for the successful alleviation of facial neuritis, physical dysfunction, pediatric cerebral palsy, chronic pain, and functional dyspepsia[8–12]. According to TCM theory, acupuncture points have been suggested to have links with specific organs, and stimulation of the acupuncture points could improve organ function and blood circulation, thereby achieving a therapeutic effect. More recently, acupuncture has been used for symptom control in cancer patients. It is helpful in reducing lymphedema, easing nausea and vomiting, and attenuating neurotoxicity in cancer patients[13–16]. But the evidence of effects on patient quality of life is conflicting[17].

The effects of acupuncture on chemotherapy-related GI symptoms in advanced gastric cancer have not yet been extensively investigated. For the present study, we recruited 56 patients with advanced gastric cancer and randomly allocated them to an acupuncture (experimental) group and a non-acupuncture (control) group for an examination of the effectiveness of acupuncture for the prevention or treatment of GI side effects resulting from chemotherapy.

METHODS

Study Cohort and Inclusion Criteria

All subjects were inpatients being treated for advanced gastric cancer at the First Affiliated Hospital of Chengdu Medical College from January 2014 to December 2015. To be included, patients had to meet these criteria:

- Age 40–70 years (either sex)
- Diagnosed with stage IV gastric cancer by gastroscopy and histopathology
- No prior surgical or chemotherapeutic treatment, or at least 1 month post surgery with no complications
- No serious heart, lung, liver, or kidney dysfunction, and serum albumin exceeding 35 g/L
- Agreed to be included in the study, with signed consent

Patients were withdrawn from the study if

- chemotherapy caused severe bone marrow suppression and led to the prescription of other medications or the termination of chemotherapy;
- chemotherapy caused severe liver or kidney dysfunction and led to the prescription of other medications or termination of chemotherapy; or
- disease progressed or proved fatal.

All procedures were conducted in accordance with the ethics standards of the responsible committee at the First Affiliated Hospital of Chengdu Medical College and with the Helsinki Declaration of 1975, as revised in 2008.

Study Design

After randomization, the experimental (acupuncture) and control (non-acupuncture) groups each included 28 patients. All patients received the standard chemotherapeutic regimen of oxaliplatin and paclitaxel (oxaliplatin 85 mg/m^2, paclitaxel 135 mg/m^2). Esomeprazole by intravenous injection (40 mg daily) was used in both groups to treat GI symptoms. Patients in the experimental group received a 30-minute session of acupuncture daily at 09h00 for 2 weeks (14 days), with 0.45×25 mm fine needles being applied at 5 acupuncture points: Zusanli, Shangjuxu, Tianshu, Sanyinjiao, and Neiguan. Before acupuncture, the skin was sterilized with 75% alcohol. Patients were checked for bleeding at the acupuncture points after each treatment.

Parameter Assessments

We assessed these parameters:

- Average hospitalization period (days) and cost
- Frequency of vomiting and diarrhea, duration of nausea, and abdominal pain by daily patient self-report (recorded and assessed by a researcher who was blind to the experiment)
- Quality of life
  The World Health Organization's WHOQOL-100 questionnaire uses 100 questions to evaluate 24 aspects of quality of life. Each question is scored from 1 to 5 ("extremely unsatisfactory" to "extremely satisfactory"). Patients completed the questionnaire at day 0 (the day before experiment) and day 14 (last day of study).
- Safety of acupuncture
  Blood was tested for white blood cells, platelets, hemoglobin, liver and kidney function, and myocardial enzymes twice weekly. The incidence rates of infection and bleeding, if any, at acupuncture points were determined.

Statistical Analysis

The statistical analyses were performed using the SPSS Statistics software application (version 17.0: SPSS, Chicago, IL, U.S.A.). Quantitative data and categorical data were evaluated by t-test and chi-square test respectively. Statistical significance was considered at $p < 0.05$.

RESULTS

Clinical Information

Of the 56 participating patients, 37 were men and 19 were women, with ages ranging from 41 to 68 years (average: 57 years). Half of the patients (18 men, 10 women) had undergone surgery for gastric cancer at least 1 month before the experiment, with no postsurgical complications. The histologic types of gastric cancer in this group included tubular adenocarcinoma, papillary adenocarcinoma, poorly differentiated adenocarcinoma, mucinous adenocarcinoma,

and signet-ring cell carcinoma. Table I presents the clinical information for the patients. All patients had been diagnosed with stage IV gastric cancer and had not received prior chemotherapeutic treatment.

Average Hospitalization Period and Cost

The average hospitalization period for the patients in the control group was 20 ± 2 days, at an average cost of ¥20,114 ± ¥473. Patients in the experimental group were hospitalized for 17 ± 2 days on average, at an average cost of ¥18,729 ± ¥421 (Table II).

Frequency and Duration of GI Symptoms

Nausea was sustained for 32 ± 5 minutes and for 11 ± 3 minutes daily in the control and experimental groups respectively. Vomiting in the experimental group occurred 2 ± 1 times daily on average compared with 4 ± 1 times daily in the control group. Abdominal pain persisted for 7 ± 2 minutes and for 16 ± 5 minutes daily in the experimental and control groups respectively. The experimental group experienced episodes of diarrhea 1 ± 1 times daily on average; the control group experienced episodes of diarrhea 3 ± 1 times daily (Table II). The differences between the groups were statistically significant ($p < 0.05$).

Quality of Life

The average score on the WHOQOL-100 quality-of-life assessment scale was 4 ± 1 for the experimental group and 2 ± 1 for the control group (Table II). The difference in quality-of-life scores between the experimental and the control groups was statistically significant ($p < 0.05$).

Safety of Acupuncture

Blood samples were drawn twice weekly from all subjects. Before chemotherapy, no significant differences in blood-sample parameters were observed between the experimental and control groups. Although the number of white blood cells and platelets slightly decreased, and mild anemia occurred in some subjects of both groups, differences between the groups were not statistically significant (Table III). No infection or bleeding at the acupuncture points was reported for patients receiving acupuncture treatment.

TABLE I Clinical characteristics of the study subjects

Characteristic	Patient group	
	Control	Intervention
Sex (*n*)		
Men	18	19
Women	10	9
Age (years)		
Range	41–68	41–67
Average	57	57
Histologic type (*n*)		
Tubular adenocarcinoma	12	11
Papillary adenocarcinoma	7	8
Poorly differentiated adenocarcinoma	6	5
Mucinous adenocarcinoma	2	3
Signet ring cell carcinoma	1	1

DISCUSSION

Our study demonstrates that TCM acupuncture can effectively relieve or mitigate the GI symptoms induced by chemotherapy in advanced gastric cancer patients. Four of the commonly seen GI symptoms—nausea, vomiting, abdominal pain, and diarrhea—were used as clinical markers, and, compared with the control group, the experimental group showed a statistically significant reduction in the frequency or duration of GI symptoms ($p < 0.05$).

If the adverse effects of chemotherapy are relieved by acupuncture, patients might be better able to withstand the entirety of their chemotherapeutic regimen, thereby improving the overall effectiveness of treatment and enhancing clinical outcomes. According to TCM theory, acupuncture points correspond to specific meridians and organs. It is theorized that stimulating specific acupuncture points can improve *chi* and blood circulation, thereby correcting organ dysfunction. In TCM, GI symptoms are often related to a functional deficiency of spleen and

TABLE II Hospitalization and gastrointestinal symptoms in the control and intervention groups

Characteristic	Patient group	
	Control	Intervention[a]
Hospitalization		
Average duration (days)	20±2	17±2
Average cost (yuan)	20,114±473	18,729±421
Duration of nausea (minutes/day)		
Day 0	2±1	2±1
Day 14	41±6	16±3
Average	32±5	11±2
Frequency of vomiting (times/day)		
Day 0	1±1	1±1
Day 14	7±2	3±1
Average	4±1	2±1
Duration of abdominal pain (minutes/day)		
Day 0	3±1	2±1
Day 14	21±4	11±2
Average	16±3	7±2
Frequency of diarrhea (times/day)		
Day 0	1±1	1±1
Day 14	5±2	2±1
Average	3±1	1±1
Quality of life score		
Day 0	4±1	4±1
Day 14	2±1	4±1

[a] Boldface type indicates $p < 0.05$ for the comparison of that value with the value for the control group.

Day 0 = the day before study; day 14 = the last day of the study; average = average of all measurements.

TABLE III Results of blood analyses before and after chemotherapy in the control and intervention groups

Analysis	Control group		Intervention group	
	Before chemotherapy	After chemotherapy	Before chemotherapy	After chemotherapy
White blood cells (10^9/L)	7.35±1.79	3.98±1.31	6.84±1.62	4.04±1.16
Hemoglobin (g/L)	141±12	122±11	137±16	121±10
Platelets (10^9/L)	217±42	99±28	203±57	102±31

stomach, which is a result of insufficient *chi* and blood. In the present study, 5 acupuncture points—Zusanli, Shangjuxu, Tianshu, Sanyinjiao and Neiguan—were selected. The Zusanli, Shangjuxu, and Tianshu points reduce GI secretions, thereby decreasing stomach and intestinal spasms to relieve pain, vomiting, and diarrhea, and the Sanyinjiao and Neiguan points regulate *chi* and replenish blood, adjusting and fortifying liver and spleen function and thereby promoting digestion and absorption to reduce symptoms such as abdominal bloating, diarrhea, and indigestion.

The WHOQOL-100 quality-of-life assessment scale covers 24 aspects of quality of life, including physiologic and psychological status, stress level, capability for daily living, work ability, household life, and religion. The comprehensiveness of the questionnaire provides a detailed reflection of the life and health status of an individual; consequently, it has been widely utilized in clinical practice[18–21]. Based on their experiences or condition during the preceding 2 weeks, subjects score each question on a scale of 1–5. Our two groups had similar scores before the study (Table II), but at end of study, scores in the experimental group were significantly higher than they were in the control group ($p < 0.05$), suggesting that acupuncture can improve a patient's quality of life.

The average periods of hospitalization were 20 ± 2 and 17 ± 2 days for the control and experimental groups respectively. Despite the difference in duration of hospitalization for the two groups being statistically nonsignificant, the 15% reduction in hospitalization time could enhance the efficiency of ward occupancy while limiting the chances of nosocomial infections developing. The average hospitalization cost was 6.89% lower for the experimental group (¥18,729 ± ¥421) relative to the control group (¥20,114 ± ¥473). Acupuncture treatments did not increase the hospitalization cost; instead, they lowered that cost compared to the cost for the control group, possibly because patients in the control group relied more on medications to manage the adverse effects of chemotherapy, such as nausea, vomiting, and diarrhea. No statistical significance with respect to the presence of GI symptoms in the two groups was evident before study start (Table II), but at the end of the study, the experimental group had experienced less vomiting and diarrhea, and shorter bouts of nausea and abdominal pain than the control group had ($p < 0.05$). The present study therefore implies that acupuncture treatment could reduce GI symptoms and hospitalization costs, thereby easing the financial burden on patients and their families, with beneficial economic and social effects.

White blood cells, platelets, hemoglobin, myocardial enzymes, and liver and kidney function were monitored for all subjects. Slight reductions in white blood cell and platelet counts and mild anemia were observed in some patients from both groups after chemotherapy, but overall, no measure was statistically significantly different between the groups. Furthermore, patients in both groups demonstrated normal liver and kidney function and normal myocardial enzyme levels, suggesting that acupuncture does not exacerbate the adverse effects of chemotherapy such as marrow suppression or liver and kidney dysfunction. Clinical guidelines released by the American Society of Clinical Oncology state that patients with a platelet level lower than 50,000/μL (normal range: 100,000–300,000/μL) should automatically be withdrawn from studies[22]. In the present study, no infection or bleeding was observed at any acupuncture point, suggesting that, as shown in previous studies[23–25], advanced gastric cancer patients who experience slight reductions in their white blood cell and platelet counts can receive acupuncture treatment safely.

CONCLUSIONS

Our study suggests that acupuncture is safe for patients with advanced gastric cancer receiving chemotherapy treatment and that it might effectively and safely reduce chemotherapy-induced nausea, vomiting, abdominal pain, and diarrhea in patients with advanced gastric cancer, thereby improving quality of life for those patients without any obvious side effects. From an economics perspective, acupuncture could reduce a patient's duration of hospitalization, thereby lowering the financial burden for that individual and increasing ward utilization efficiency. We think that acupuncture is a safe and effective intervention that could be beneficial during clinical treatment for cancer. However, in this preliminary study, the small sample size and the lack of a placebo comparator probably affected the study results. Basic theoretical study in this field is still insufficient, and the all-important large clinical studies are lacking. We need more and further scientific research into the clinical use of acupuncture to relieve the adverse effects of chemotherapy.

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CONFLICT OF INTEREST DISCLOSURES

We have read and understood *Current Oncology*'s policy on disclosing conflicts of interest, and we declare that we have none.

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