RESEARCH ARTICLE

Acupuncture as a Complementary Treatment for Cancer Patients Receiving Chemotherapy

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Abstract

Background: Medical treatment for eliminating the side effects of cancer therapy may not always be efficacious. Acupuncture is one of the most widely accepted alternative and complementary therapies in use today. In this study, we investigated the efficacy of acupuncture in patients experiencing cancer treatment side effects, including nausea, vomiting, pain, poor sleep quality and anxiety. Materials and Methods: A total of 45 inpatients who underwent chemotherapy between February and April 2013 in the Oncology Department of Numune Hospital were included in our study. Acupuncture was administered to the patients one day prior to chemotherapy, on the day of chemotherapy and one day after chemotherapy. The patients were evaluated on nausea, vomiting, pain, sleep quality and anxiety before the chemotherapy and on the 4th day of chemotherapy. Results: Of the 45 patients included in the study, 18 (40%) were female and 27 (60%) were male. A total of 25 (55.6%) had an elementary school education; 32 patients (71%) had stage 4 cancer and were treated with palliative chemotherapy (the patient characteristics are shown in Table 1). Statistically significant decreases ($p<0.001$) in pain, nausea, vomiting, insomnia and anxiety scores were observed after the acupuncture treatment compared to baseline. There were no differences in the age, gender, education level, stage or metastasis levels between the patient groups whose symptoms improved or were unchanged. Conclusions: Our study showed that acupuncture has positive effects in cancer treatment patients who experience nausea, vomiting, pain, poor sleep quality and anxiety as side effects of chemotherapy. Chemotherapy-related side effects in cancer patients could be decreased by the concurrent use of acupuncture.

Keywords: Acupuncture - cancer - chemotherapy - nausea - insomnia - anxiety - vomiting - pain - Turkey

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Introduction

Cancer treatment is accompanied by many side effects that are not eliminated by current medical approaches. In addition to medical treatment, Complementary and Alternative Medicine (CAM) is beneficial. The CAM therapies that alleviate or eliminating the side effects of cancer treatment in these patients are becoming increasingly popular. Lee et al. stated that more than 40% of the patients who were diagnosed with cancer received CAM therapies (Lee et al., 2000). Among these methods, acupuncture is one of the most commonly used (Johnstone et al., 2002).

Acupuncture for different indications could be clinically significant in patients with different types of cancer. From results of randomized controlled trials, it has been shown that palliative care patients benefited from acupuncture in most of the examined studies (Standish et al., 2008). In this meta-analysis, acupuncture is shown to reduce to varying degrees the major side effects of chemotherapy and radiation therapy.

The nausea and vomiting associated with chemotherapy for cancer is a significant problem in 75% of the patients (Roscoe et al., 2000). In most of the acupuncture studies, acupuncture was used for the prevention of nausea and vomiting in cancer patients, and the results were successful to varying degrees (Ezzo et al., 2006). It may reduce cancer-related fatigue (He et al., 2013).

Acupuncture is also used to relieve pain in cancer patients, especially head, neck, abdomen and chest pain, and ear acupuncture is effective in the neuropathic pain of cancer patients (Alimi et al., 2003). In a study conducted in 286 patients with bone metastasis, the use of analgesic or sedative drugs decreased (Guo et al., 1995).

Because of the anxiolytic and sedative effects of acupuncture, symptoms of nervousness and insomnia in cancer patients decreased (Lin et al., 2012). Limited studies related to anxiety and depression in cancer patients are available, however, acupuncture is effective an antidepressant treatment in non-cancer patients (Cohen et al., 2005).

In this study, we aimed to investigate the effect of acupuncture on nausea, vomiting, pain, sleep quality, and anxiety in cancer patients who underwent chemotherapy or were hospitalized.

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Materials and Methods

A total of 45 chemotherapy patients in the Medical Oncology Department of Ankara Numune Training and Research Hospital (ANTRH) between February 2013 and April 2013 were enrolled in the study. The ANTRH Ethics Committee approved the study. The patients were informed about the aim of the study, and volunteer and recognizant patients were included in the study. All of the patients were over 18 and diagnosed with cancer. The patients that would be hospitalized for at least 3 days and would receive chemotherapy during the hospitalization were selected for the study. The diagnosis, gender, education, treatment methods and disease stage were not taken into account. The study exclusion criteria were high fever, signs of infection, bleeding diathesis, thrombocytopenia and the absence of any antiplatelet or anticoagulant medication.

The patients were evaluated for pain, nausea, vomiting, sleep quality and anxiety before and after acupuncture.

The patients received acupuncture on 3 days starting on the day of admission to the hospital. The pain intensity was assessed by the Visual Analogue Scale (VAS) before and after series of acupuncture treatments. The oral intake and vomiting of the patients during the first 24 hours after chemotherapy were noted with respect to the VAS in Table 1. Identical questions were asked after the acupuncture treatments during chemotherapy and after the following 24 hours. Nausea (according to the oral intake) and vomiting were graded between 0 and 4 in Table 1. A decline of at least one degree after acupuncture was considered statistically significant in the ratings of nausea and vomiting.

The patients were assessed with the Insomnia Severity Index (Bastien et al., 2001) on the day of hospitalization and after the administration of acupuncture on 3 days. [The scale was validated for Turkish populations (Boysan et al, 2010). According to the index, insomnia severity was scored by asking 7 questions. A total score of 0 to 7 was evaluated as the absence of insomnia, whereas 8 to 14 as sub-threshold, 15 to 21 as moderate and 22 to 28 as severe insomnia. A decline of at least one degree in insomnia severity after the administration of acupuncture was considered statistically significant.

On the day of hospitalization and after the administration of acupuncture for 3 days, the anxiety status of patients were graded as mild, moderate of severe using the Beck Anxiety Scale (Beck et al., 1988) [The scale was validated for Turkish populations (Ulusoy et al., 1998)]. A total of 21 questions were asked, and they were scored between 0 and 3. A total score of 0-21 was evaluated as mild anxiety, whereas 21-42 was moderate and 42-63 total score was severe. A decline of at least one degree in the anxiety level after the administration of acupuncture was considered statistically significant.

Acupuncture was administered to the patients on 3 consecutive days as follows: one day prior to chemotherapy, on the chemotherapy day and one day after chemotherapy. Acupuncture was performed by an experienced licensed physician acupuncturist on 3 consecutive days between 11-12 a.m. The LI4, PC6, H7, ST36 and Liv3 points were needled bilaterally with 0.25×25 mm, sterile disposable steel needles that were removed after 20 minutes. All of the questionnaires and inquiries were repeated on the 1st and 4th day of hospitalization.

Statistical analysis

The data analysis was performed using SPSS for Windows, version 11.5 software (SPSS, Inc., Chicago, IL, USA). The metric discrete variables were shown as the mean±SD, and the median (25^{th}-75^{th} percentiles) were used for the ordinal variables. The categorical data were expressed as the number of cases and (the%).

The differences between the pre and post-acupuncture clinical scores (i.e., the VAS and the levels of vomiting, nausea, insomnia and anxiety) were evaluated by the Wilcoxon Sign Rank test. The mean age differences between the groups were compared by Student's t-test; the Mann-Whitney U test was applied for the comparisons of education level and cancer stage. The nominal data were analyzed by Pearson's Chi-square or Fisher's exact test, where appropriate.

Multiple logistic regression analysis was used to determine the independent predictors, which typically affected recovery from insomnia. Any variable whose univariable test had a p value <0.25 was accepted as a candidate for the multivariable model with all of the variables of known clinical importance.

A p value less than 0.05 was considered statistically significant.

Results

Of the 45 patients included in the study, 18 (40%) were female, and 27 (60%) were male; 25 (55.6%) patients were primary school graduates, and 32 patients (71%) were at stage 4 of cancer and receiving palliative care. Whereas 36 of the 45 patients were recurrent chemotherapy patients, 9 patients received chemotherapy for the first time. The effect of acupuncture on nausea and vomiting was not evaluated for the first time chemotherapy patients. Table 2 shows the demographic characteristics of the patients.

Compared to the pre-treatment levels, in terms of the VAS, nausea scores and anxiety level, no statistically significant difference was observed (p>0.05) between the improved and invariant groups after treatment by age, gender, education level, stage and metastasis. No further analysis was conducted because all of the factors, excluding metastasis, had a significance level over 0.25.

Compared to pre-treatment, in terms of the insomnia

Table 1. Visual Analogue Scale

	Grade 0	Grade 1	Grade 2	Grade 3	Grade 4
Nausea	Oral intake	Oral intake poor	Oral intake very poor	No oral intake	Continuous nausea
Vomiting/days	None	1	1-5	6-10	More than 10

Table 2. Demographic and Clinical Characteristics of All Cases

Variables		n=45
Age		50.5±13.3
	Age interval	20-79
Sex	Male	18 (40.0%)
	Female	27 (60.0%)
Educational status	Illiterate	9 (20.0%)
	Primary school graduate	25 (55.6%)
	Junior high school graduate	1 (2.2%)
	High school graduate	9 (20.0%)
	University graduate	1 (2.2%)
Diagnosis	Stomach ca.	13 (28.9%)
	Breast ca.	7 (15.6%)
	NHL	7 (15.6%)
	Colon ca.	6 (13.3%)
	Head-neck ca.	3 (6.7%)
	NSCLC	3 (6.7%)
	Sarcoma	3 (6.7%)
	Pancreatic ca.	2 (4.4%)
	CUP.	1 (2.2%)
Stage	I	1 (2.2%)
	II	3 (6.7%)
	III	9 (20.0%)
	IV	32 (71.1%)
Treatment type	Adjuvant chemotherapy	13 (28.9%)
	Palliative chemotherapy	32 (71.1%)

*NHL: Non-Hodgkin Lymphoma; NSCLC: Non-Small Cell Lung Cancer; CUP: Cancer of Unknown Primary

Table 3. Distribution of Cases According to the Changes in Scores of VAS, Nausea, Vomiting, Insomnia and Anxiety Before and After Treatment

Variables	Invariant	Improved after treatment
VAS	21 (46.7%)	24 (53.3%)
Nausea	10 (27.8%)	26 (72.2%)
Vomiting	17 (47.2%)	19 (52.8%)
Insomnia	26 (57.8%)	19 (42.2%)
Anxiety	19 (42.2%)	26 (57.8%)

*VAS: Visual Analogue Scale

Table 4. Distribution of Cases According to the Status of Insomnia and Anxiety Before and After Treatment

Variables		Pre-treatment	Post-treatment
Insomnia	None	16 (35.6%)	21 (46.7%)
	Subthreshold	9 (20.0%)	9 (20%)
	Moderate	9 (20.0%)	15 (33.3%)
	Severe	11 (24.4%)	0 (0.0%)
Anxiety	Mild	15 (33.3%)	37 (82.2%)
	Moderate	23 (51.1%)	7 (15.6%)
	Severe	7 (15.6%)	1 (2.2%)

scores, no statistically significant difference was observed (p>0.05) between the improved and invariant groups after treatment by age, gender, education level, stage and metastasis. Concerned that the age and educational status was evaluated to be effective in further analysis (p<0.25), age and education level were assessed together, and their effects on the insomnia score improvement were investigated in the next step. As a result of the multivariate analysis, the assessment of the combination of age and education level had no statistically significant effect on the insomnia improvement scores (p>0.05).

Compared to pre-treatment, a statistically significant decrease (p<0.001) was observed in all VAS, nausea, vomiting, insomnia and anxiety scores.

Table 5. Distribution of Cases According To The Demographic Characteristics Because of Changes In Scores of VAS, Nausea, Vomiting, Insomnia and Anxiety Before and After Treatment

Variables	Invariant	Improved	p value
VAS	n:21	n:24	
Age	52.3±4.7	48.6±11.8	0.297†
Sex M/F	8 (38.1 %)/13 (61.9 %)	10 (41.7 %)/ 14 (58.3 %)	0.807‡
Educational Stat.: I/P/JHS/HS/U	5/9/0/7/0	4/16/1/2/1	0.614¶
Stage: I/II/III/IV	0/2/6/13	1/1/3/19	0.258¶
Metastasis	13 (61.9 %)	19 (79.2 %)	0.202‡
Nausea	n:10	n:26	
Age	47.0±10.5	51.6±13.8	0.343†
Sex M/F	3 (30.0 %)/7 (70.0 %)	11 (42.3 %)/15 (57.7 %)	0.706#
Educational Stat.: I/P/JHS/HS/U	2/4/1/3/0	4/17/0/5/0	0.590¶
Stage I/II/III/IV	0/0/3/7	0/2/3/21	0.715¶
Metastasis	7 (70.0 %)	21 (80.8 %)	0.658#
Vomiting	n:17	n:19	
Age	50.7±10.5	50.0±15.0	0.883†
Sex M/F	5 (29.4 %)/12 (70.6 %)	9 (47.4 %)/10 (52.6 %)	0.270‡
Educational Stat.: I/P/JHS/HS/U	3/9/1/4/0	3/12/0/4/0	0.827¶
Stage I/II/III/IV	0/0/5/12	0/2/1/16	0.594¶
Metastasis	12 (70.6 %)	16 (84.2 %)	0.434#
Insomnia	n:26	n:19	
Age	53.0±11.7	47.2±14.8	0.153†
Sex M/F	11 (42.3 %)/15 (57.7 %)	7 (36.8 %)/12 (63.2 %)	0.712‡
Educational Stat.: I/P/JHS/HS/U	8/13/1/4/0	1/12/0/5/1	0.050¶
Stage I/II/III/IV	1/1/7/17	0/2/2/15	0.394¶
Metastasis	17 (65.4 %)	15 (78.9 %)	0.321‡
Anxiety	n:19	n:26	
Age	50.3±13.4	50.7±13.4	0.926†
Sex M/F	9 (47.4 %)/10 (52.6 %)	9 (34.6 %)/17 (65.4 %)	0.388‡
Educational Stat.: I/P/JHS/HS/U	5/8/1/4/1	4/17/0/5/0	0.919¶
Stage I/II/III/IV	1/2/5/11	0/1/4/21	0.080¶
Metastasis	11 (57.9 %)	21 (80.8 %)	0.094‡

*M/F: Male/Female, I/P/JHS/HS/U: Illiterate/Primary/Junior High School/High School/University, †: Student's t-Test, ‡: Pearson's Chi-square Test, ¶: Mann-Whitney U Test, #: Fisher's Exact Chi-square

Table 6. The Scores of VAS, Nausea, Vomiting, Insomnia and Anxiety Before After Treatment

Variables	Pre-treatment	Post-treatment	p value*
VAS	5 (2-8)	2 (1-5)	<0.001
Nausea	2 (1-3)	0.5 (0-1)	<0.001
Vomiting	1.5 (1-2)	1 (0-1)	<0.001
Insomnia	1 (0-2.5)	1 (0-2)	<0.001
Anxiety	1 (0-1)	0 (0-0)	<0.001

*Wilcoxon Signed-Rank Test; **Data shown in the form of media (25.percentile-75. percentile)

Discussion

Many cancer patients use a CAM therapy during or after treatment. Acupuncture, which is a CAM method, is widely used to eliminate the side effects of chemotherapy in cancer patients and in palliative care (Towler et al., 2013).

With the increase in the number of surviving cancer patients after intensive treatment, there is also an increase in the incidence of side effects. Acupuncture is effective in the treatment and management of the side effects of chemotherapy and radiation therapy. A single session of acupuncture treatment could be beneficial for cancer

treatment side effects such as nausea, vomiting, dry mouth and constipation, as well as for pain, depression and anxiety (Lin et al., 2012; Cohen et al., 2013).

In this study we aimed to investigate the effect of acupuncture on nausea, vomiting, pain, sleep quality, and anxiety in cancer patients who undergo chemotherapy or inpatient treatment. The oncology patients hospitalized for chemotherapy had acupuncture with a combination of more than one point in the same session in a holistic treatment approach. When we evaluated the results of our study, a statistically significant decline in symptoms of the patients was detected.

Nausea is a common side effect of chemotherapy. The intensity and frequency of nausea was found to decrease after acupuncture following the administration of an antiemetic in rheumatic patients who received chemotherapy in a study by A. Josefson et al. The number of patients vomiting during the current hospitalization decreased compared to during the previous chemotherapy (Josefson and Kreuter, 2003).

In a study by Vickers et al. in breast cancer patients receiving high-dose chemotherapy, with the addition of acupuncture to conventional therapy, symptoms of nausea and vomiting decreased in patients compared to the placebo group (Vickers et al., 2004). In another study, a group of patients who received high-dose chemotherapy after bone marrow transplantation were administered acupuncture with ondansetron; comparing the acupuncture group with the placebo group, acupuncture was not beneficial in the prevention of chemotherapy-induced nausea and vomiting (Streitberger et al., 2003).

In our study, a comparison of the levels of nausea and vomiting of the patients after the previous chemotherapy session with the levels of nausea and vomiting of the patients receiving chemotherapy with acupuncture showed that the symptoms were decreased in 72.2% of the patients with nausea and in 52.8% of patients with vomiting.

Acupuncture point PC6 is typically used to treat nausea and vomiting. Ezzo J et al. found that acupressure, electro-acupuncture or acupressure at PC6 was useful for treating nausea and vomiting. Other studies (Ezzo et al., 2006) are needed, however, we effectively used points PC6 and ST36 together to treat nausea and vomiting.

In a study with fMRI, an increase in signaling was detected in the hypothalamus, insula, and cerebellum (the nodulus portion and uvula) of the brain by stimulating the PC6 point. With this study, the sedative effect observed in the clinic during acupuncture for nausea at the PC6 point is also shown in the laboratory (Bai et al., 2010). In our study, the HT7 and Liv3 points were used to increase the sedative effect of acupuncture at PC6. A decline in anxiety levels and the severity of insomnia in the patients was detected.

Acupuncture is useful for reducing the severity of anxiety (Pilkington et al., 2007). In our study, the rate of serious anxiety decreased from 15.6% to 2.2% before and after acupuncture, respectively. There was a 57.8% reduction in the severity of anxiety in all of the patients.

In Germany, acupuncture in patients with minor depression was superior to sham acupuncture (Eich et al., 2000). Zhang et al. compared acupuncture and doxepin, an anxiolytic, for anxiety and found that the results were similar (Zhang et al., 2003). The effect of acupuncture on symptoms such as nausea, vomiting and pain as well as anxiety and the mood status of cancer patients was evaluated and reported to be useful in other studies (Cohen et al., 2005; Lu et al., 2008; Towler et al., 2013).

Acupuncture for vasomotor symptoms and mood disorders in breast cancer patients was more efficient than relaxation therapy and was effective for vasomotor symptoms, anxiety and insomnia by increasing endogenous opioids, including beta-endorphin and serotonin (Sok et al., 2003). Patients reported that the severity of insomnia decreased after acupuncture;11% of severe insomnia was eliminated after acupuncture.

Although Cheuk DK et al. found acupuncture useful in some studies, they did not recommend it for the treatment of insomnia because of the studies were poorly designed and heterogeneous (Cheuk et al., 2012). In another review, acupuncture was effective in reducing insomnia (Sok et al., 2003). In the study conducted by Cheng CH et al., there was an increase in NREM sleep in rats after electro-acupuncture. (Cheng et al., 2011).

Another study reported that acupuncture improved the quality and duration of sleep and increased melatonin in 18 patients suffering from insomnia and anxiety symptoms. Although the entire interaction is unknown, it is hypothesized that melatonin interacts with opioid peptides. Acupuncture is useful in the treatment of anxiety and insomnia because of its effect on the dopaminergic and serotonergic neurons and the opiate system as well as for its pain relief feature. These effects tend to interact with each other (Spence et al., 2004; Yano et al., 2004; Nedstrand et al., 2006).

The studies related to insomnia were not conducted specifically as anxiety studies in cancer patients. These symptoms were evaluated with several symptoms in cancer patients, as in our study, and acupuncture was cited as useful in treating the anxiety and sleep problems frequently seen in patients diagnosed with cancer (Nedstrand et al., 2006; Standish et al., 2008; Lin et al., 2012; Towler et al., 2013).

In the USA, 75% of advanced cancer cases receive pain treatment. In Europe, it was found that 72% of cancer patients suffer from pain. In a review by Choi TY et al., acupuncture was shown to reduce the necessary dosage of painkillers in some randomized controlled studies, although in other studies, the effect of acupuncture for cancer pain was reported to be very limited (Choi et al., 2012). In our study, we found that acupuncture is useful in reducing pain complaints in patients with cancer.

Opioid-based analgesics are mainly used for cancer pain, and these have serious side effects such as nausea and constipation. Because acupuncture has very few side effects, it is preferred for cancer pain. Although acupuncture is commonly used in palliative treatment centers, the evidence level for cancer pain was found to be low (Paley et al., 2011). The National Comprehensive Cancer Network Guide suggests the use of acupuncture with conventional therapy for cancer (Lu and Rosenthal, 2013). In the study by Chan et al., better results were obtained in the acupuncture treatment group compared

to the group of cancer patients who received different analgesics according to the severity of pain (Chen et al., 2008). A positive change in pain levels and the quality of life of 8 cancer patients who received acupuncture treatment was reported in a study by Vinjam SP et al. (2013).

A reduction in pain complaints after acupuncture was reported in a group of 28 cancer patients with benign soft tissue pain, neuropathic pain, and benign and malignant bone pain (Leng, 1999).

After acupuncture, a decrease in pain intensity was detected in 53.3% of the patients reporting pain. Seventy-one percent of our patients were diagnosed with metastatic cancer, and it was assumed that the pain of these patients was probably cancer pain. The etiology of the pain was not determined in our study.

In our study, the results obtained in terms of nausea, vomiting, anxiety, insomnia and pain were not affected by the characteristics of the patients' demographics (age, gender, education level) or the stage of the disease. Our results would probably have been different if the effect of demographic characteristics could be evaluated with more patients.

A single session of acupuncture treatment was found to benefit patients with nausea, vomiting, anxiety, insomnia and pain as side effects of chemotherapy for cancer. We hypothesize that acupuncture treatment with a holistic approach might be useful in oncology centers because it causes fewer side effects than conventional treatments.

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