

# Acupuncture is an Effective Supportive Treatment Method in the Prevention of Chemotherapy Induced Nausea and Vomiting

## Akupunktur, Kemoterapi Alakalı Gelişen Bulantı ve Kusmanın Önlenmesinde Etkili Bir Destek Tedavi Yöntemidir

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### Abstract

**Objective:** Nausea and vomiting are the main problems affecting life quality of patients receiving chemotherapy. Thus, after obtaining institutional ethics committee approval and patients' informed consent, the effect of acupuncture on nausea and vomiting in addition to classical antiemetic treatment was studied.

**Material and Method:** Patients who have experienced vomiting and nausea during the first course of the treatment despite the pharmacological treatment have been interviewed in their visits during the second course and been included into the study. In the study group 80% of patients were female; 23% of patients had breast cancer, 13% had colorectal cancer, 64% had other cancer types.

**Results:** Nausea and vomiting totally disappeared in 30% of the patients where acupuncture was used as an additional treatment strategy (p:0.001). No correlation was found between diagnosis, gender, age group and response to acupuncture. It has been detected that women who had more severe pregnancy nausea experienced less response to pharmacological antiemetic treatment.

**Conclusion:** If classical antiemetic modality is not adequate to prevent nausea and vomiting, acupuncture is advised in addition to antiemetics as an effective method.

**Key Words:** Acupuncture, Chemotherapy, Nausea, Vomiting

### Özet

**Amaç:** Bulantı ve kusma, kemoterapi uygulanan hastalarda hayat kalitesini etkileyen en önemli etkenlerdir. Bu görüşten hareketle, yerel etik kurul ve katılan hasta onayları alındıktan sonra, akupunkturun klasik antiemetik tedaviye ek olarak etkisi araştırıldı.

**Gereç ve Yöntem:** Tedavilerinin ilk kürü sırasında klasik farmakolojik tedaviye karşın bulantı ve kusmadan muzdarip olanlar, ikinci kür tedaviye geldiklerinde karşılıklı görüşülerek çalışmaya dahil edildiler. Hastaların %80'i kadınlardan oluşurken, %23'ü meme kanseri, %13'ü kolorektal kanser ve %64'ü de diğer kanser tanılarına sahipti.

**Bulgular:** Akupunkturun ek tedavi stratejisi şeklinde uygulanması ile bulantı ve kusmanın %30 olguda tamamen geçtiği görüldü (p:0.001). Akupunktura yanıt ile tanı, cinsiyet ve yaş grupları arasında herhangi bir korelasyon saptanmadı. Gebelik sürecinde şiddetli bulantısı olan hastaların klasik antiemetik tedaviye daha az yanıt verdiği dikkat çekti.

**Sonuç:** Klasik antiemetik tedavinin bulantı ve kusmayı önlemede yetersiz kaldığı durumlarda, antiemetik tedaviye ek olarak, akupunktur etkili olabilecek bir tedavi yöntemi olarak önerilebilir.

**Anahtar kelimeler:** Akupunktur, kemoterapi, bulantı, kusma

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### Introduction

Chemotherapy induced nausea and vomiting (CINV) is a recognized adverse effect of cancer treatment and one that is frequently cited by patients as one of their most common fears before embarking on a treatment course (1). As well as having an unfavorable effect on quality of life, CINV can also cause physiological impairment, loss of functional ability and a decrease in performance status (2,3).

CINV mostly receives less interest in practice than the primer treatment. Although it has a crucial impact, it might cause dose decrease in the primer treatment or obstruct the total primer treatment. Lately studies have been going on in order to produce more effective treatment policies. Besides these, acupuncture seems to be an effective choice as a long used wellness method.

According to Chinese tradition, the practice of acupuncture is based on the philosophy of balance and unity between the universe, living beings and energy

flow (4). The primary aim of acupuncture is the recovery of a harmonized, balanced state of the body (5). Investigators suggest that acupuncture may reduce emesis induced by chemotherapy, surgical trauma and pregnancy.

We decided to use acupuncture addition to primer treatment in cases where there was no adequate response to antiemetic treatment. Our treatment strategy was to effectively decrease CINV and to apply the primer cytotoxic treatment on time without interruption and increase the quality of life.

**Material and Methods**

Patients:

Study included 30 patients treated in Medical Oncology Inpatient Service, between October 2009 and April 2011. Patients who have experienced vomiting and nausea during the first cure of the treatment despite the pharmacological treatment have been interviewed in their visits during the second cure and included into the study. Demographic characteristics and diagnosis of the patients are shown in Table 1.

*Table 1. Demographic characteristics and diagnosis of the patients*

N=30	N
<b>Gender M/F</b>	9/21
<b>Age, years</b>	21-30: 3 31-40: 4 41-50: 6 ≥51: 17
<b>Educational status</b>	High School: 23 University: 7
<b>Diagnosis</b>	Breast: 11 Pulmonary: 7 Colorectal: 4 Nasopharynx: 4 Endometrium: 1 Gastric: 1 Cervix: 1 Biliary duct: 1

Participation was on a voluntary basis. Patients who had no visual or hearing disability or cognitive dysfunction; who were able to complete the study’s questionnaires and could speak Turkish were included in the study. The patients who agreed to participate in the study were contacted by the medical oncologist and asked to fill in a study protocol at a chemotherapy session. All patients were informed about the acupuncture as a treatment in general and its possible beneficial effect on CINV. Exclusion criteria were severe psychiatric illness, possible sensitivity to needle sticks related to hyperesthesia or allergy and lymphatic edema in the arms. Additionally; hemorrhagic diathesis and

hypercoagulability conditions were examined and patients with proper clinical and laboratory results were chosen as subjects.

Method:

Patients who were subjected to chemotherapy and classical antiemetic medical treatment (recommended by the American Society of Clinical Oncology) similar to the prior applications also received acupuncture.

The criteria for “Private health institutions and application of acupuncture treatment” described by the Ministry of Health have been followed and applied by a certified acupuncturist under the supervision of a medical oncologist.

The acupuncture points that have been widely used for nausea and vomiting control are P6, ST36, auricular points, lung, liver, spleen and stomach (Wei), and wrist points LU9, H7 (1). P6 (neiguan) is located between the tendons of palmaris longus and flexor carpi radialis at 2-body-inches proximal to the wrist crease. The acupuncture points chosen were the P6, lung and stomach on the ear, LU9 and H7 on the wrist for this study (Figure 1). These points are considered to be equal in their effect on nausea and vomiting. Special titanium disposable acupuncture needles were inserted into the patients bilaterally at least 15-30 minutes before the chemotherapy infusion was started. The normal time for acupuncture was 30-45 minutes. The area where acupuncture was applied was carefully determined while the areas with active infection, radiation burn, any open surgical wound or at the site of tumor metastasis were excluded.

*Figure 1. Acupuncture points chosen on wrist*



Questionnaires were formed according to the risk factors affecting CINV and were used to collect data while being included to the study followed by an interview.

Questionnaires consisted of four parts: diagnostics related to primer disease, ongoing treatment, vomiting and nausea conditions and agents used, sites of application of acupuncture. Vomiting-nausea conditions have been evaluated by using National Cancer Institute

(NCI) Common Terminology Criteria for Adverse Events (CTCAE) version 3.0. Chemotherapy protocols patients received and the vomiting-nausea evaluation are presented in Table 2.

Table 2. Treatment protocols and assessment of risk for nausea and vomiting

N=30	Treatment protocols	N-V Risk (%)
11	CA: Cyclophosphamide + doxorubicin	90 ↑
4	Radiotherapy + cisplatin (weekly)	30 – 90
2	Cisplatin + gemcitabine	90 ↑
1	CAF: Cyclophosphamide + doxorubicin + 5-fluorouracil	90 ↑
1	FOLFIRI (leucovorin calcium, 5-fluorouracil, irinotecan hydrochloride) + bevacizumab	30 – 90
1	IMA: Ifosfamide + mesna + doxorubicin	30 – 90
1	Radiotherapy + 5-fluorouracil + folinic acid (5 days)	10 – 30
1	TCF: Docetaxel + carboplatin + 5-fluorouracil	90 ↑
1	Carboplatin + paclitaxel	10 – 30
1	FOLFOX4: Oxaliplatin + leucovorin + 5-fluorouracil	30 – 90
1	Cetuximab + irinotecan	30 – 90
5	Cisplatin + etoposide	90 ↑

N-V: Nausea-vomiting

Statistical Analysis:

Statistical analyses were performed using McNemar test with SPSS software for Windows (Statistical Product and Service Solutions, version 15.0, SSPS Inc, Chicago, IL, USA). All p values were based on a 2-tailed test of significance (p:0.05).

**Results**

Questionnaires including CINV data were evaluated at the end of the study. All patients included in this study had severe CINV during the first cure applications and

later on. Nausea and vomiting totally disappeared in 30% of the patient population where acupuncture was used as an additional treatment strategy (p:0.001) (Figure 2). Before the acupuncture treatment 13 and 4, patients were detected with grade 2 and 3 nausea respectively. During acupuncture treatment, only 1 patient was determined to have grade 2 nausea (p<0.05) (Figure 3). No patient with grade 3 nausea was detected during acupuncture treatment. Similarly, before acupuncture treatment 7 and 4 patients were determined with grade 2 and 3 vomiting respectively. During acupuncture treatment only 1 patient was detected with grade 2 vomiting. No patient was detected with grade 3 vomiting (p<0.05) (Figure 4).

Figure 2. Percentage of nausea and vomiting before and during acupuncture (%) (p=0.001)

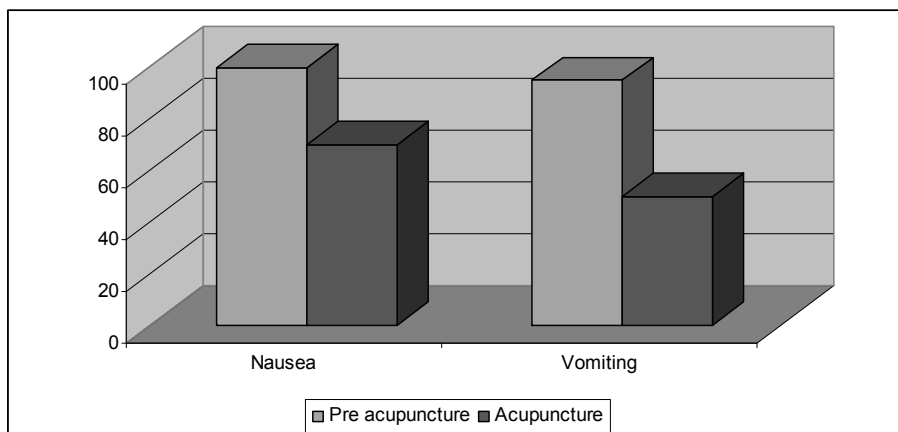


Figure 3. Assessment of nausea before and during acupuncture ( $p<0.05$ ) ( $n=30$ )

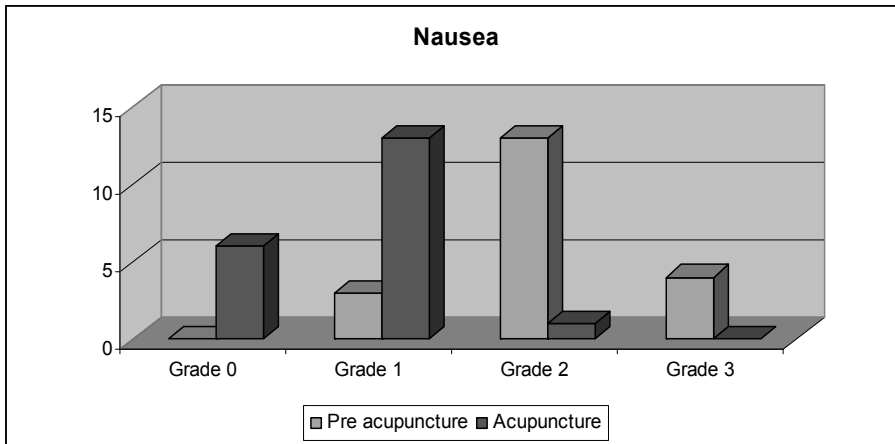
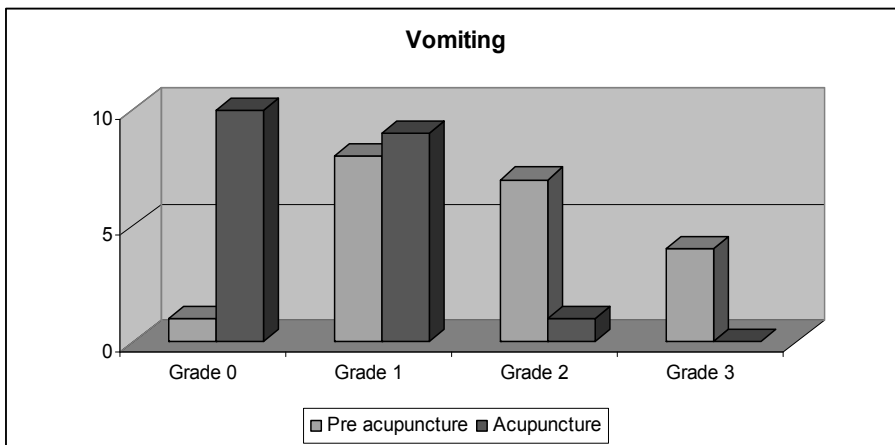


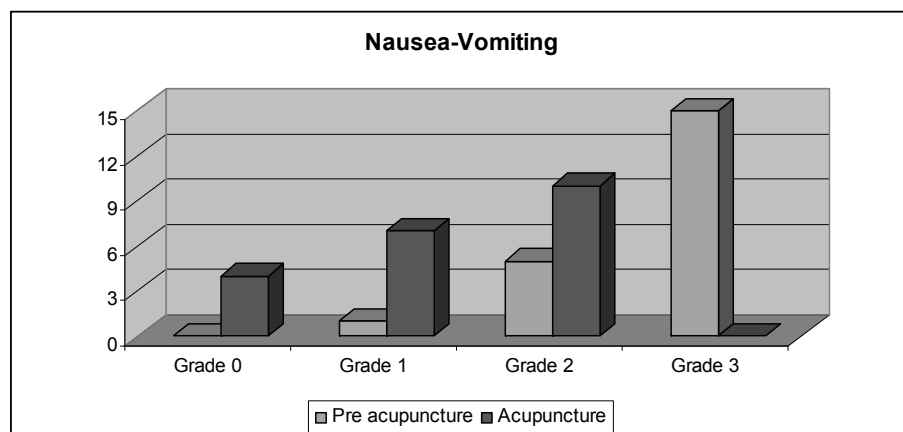
Figure 4. Assessment of vomiting before and during acupuncture ( $p<0.05$ ) ( $n=30$ )



No correlation was found between diagnosis, gender, age group, response to acupuncture and sites where acupuncture was applied. 21 women have been questioned about their pregnancy. It was detected that women who had more severe pregnancy nausea experienced less response to pharmacological antiemetic treatment, and interestingly, in this group, favorable results with acupuncture treatment were detected ( $p<0.05$ ).

Patients who received chemotherapeutic agents with high emetogenic potential such as anthracycline and cisplatin displayed vomiting grade 2 and 3. Vomiting grade decreased to grade 1 and 2 respectively when acupuncture was applied ( $p<0.05$ ) (Figure 5). At the same time, no statistical relation was found between effects of chemotherapeutics with different emetogenic potential and acupuncture response ( $p>0.05$ ).

**Figure 5.** Assessment of nausea before and during acupuncture in group of patients getting anthracycline and cisplatin which are highly emetogenic ( $p < 0.05$ ) ( $n = 20$ )



Adverse events of acupuncture included exacerbation of depression, hypertensive crisis, vasovagal reaction, asthma attack and pneumothorax. None of our patients experienced such adverse effects. The most common minor adverse events including local bleeding and sharp pain reported in the literature wasn't seen in any patients (7).

## Discussion

Compared with the routine efficient pharmacological antiemetic treatment, it seems that acupuncture combined with these agents significantly decreased both the severity and duration of CINV.

The traditional theory of acupuncture is based on the regulation of "qi" (energy) dysfunction by the stimulation of acupuncture points on the body with needles, heat or pressure (8). The details of the underlying mechanisms of acupuncture on nausea and vomiting are largely unknown. However, scientific research has demonstrated that the implementation of acupuncture needles and stimulation of acupuncture points mediates the nervous system through local effects on connective tissue, release of neurotransmitters and modulation of central nervous system activation as demonstrated by functional magnetic resonance imaging. Investigators are continuing to try and elucidate these mechanisms (8,9,10). In the oncology setting, acupuncture is proven to be effective in amelioration of CINV as determined by the National Institutes of Health (NIH) (8). The reliability of the acupuncture is as important as its effectiveness. Acupuncture needles are regulated as a medical device according to the United States Food and Drug Administration (FDA). In the study, approved disposable acupuncture needles were used.

In a review where 11 randomized controlled studies were evaluated, summarized some beneficial effects of

acupuncture point stimulation on CINV in adult cancer patients with the antiemetic regimen (11). There was decrease in CINV through acupuncture using the acupoints P6 and ST36 in three different studies which included only breast cancer patients (12,13,14). In a study on gynecological cancer patients, it was found that acupressure applied using a wristband for five days on the P6 acupuncture point on the wrists, had a significant effect in decreasing both acute and delayed CINV (15).

In another study in which the effectiveness of acupuncture on cancer patients receiving cisplatin treatment was investigated, acupuncture was found to be effective on nausea and vomiting management when combined with classic antiemetic treatment (16). In a study including 100 subjects with metastatic solid tumors who did not benefit from classic antiemetics such as corticosteroids, antidopaminic agents and serotonin receptor-antagonists in their previous treatment phase, emetic symptomatology was reduced by acupressure in 68% of the patients, without significant differences in relation to tumour histotype (17). We have seen similar results between patients treated with anthracycline-cisplatin and others; while Gardani et al. reported that the lowest efficacy was observed in patients treated by anthracycline-containing regimens.

Choo et al. reported significant decrease in nausea and vomiting incidence in 26 patients in comparison with previous classic antiemetic treatment regimes in 27 patients (18). In a review including 11 studies with 1247 cases, it was reported that stimulation with needles reduced proportion of acute vomiting but not acute nausea severity (19).

It was an expected finding to have a positive correlation between present CINV and nausea-vomiting condition of women during their past pregnancy. The use of acupuncture being effective independent from the nausea and vomiting experience is of significance. No selectivity

of acupuncture method on diagnosis of disease, stage of disease or chemotherapy type was detected in subjects included in this study.

As can be seen, many studies stand out showing that nonpharmacologic treatment has an effect on CINV such as manual needling, needling combined with electric stimulation, wrist bands, stimulation, magnetic stimulation, lasers or heat with burning herbs, applying pressure to the acupoint (acupressure) and auricular acupuncture. However, most of the clinical trials are methodologically weak (20). Common defects include an insufficient control of nonspecific effects, inadequate control interventions and small sample sizes.

The current study has some limitations. It is not a randomized-controlled study and has relatively low subject numbers. Lack of presentation about disease diagnosis and disease stages, not selecting groups according to chemotherapeutics homogeneous distribution are also some of the limitations. However it is found to be meaningful to present that manual needling acupuncture supports pharmacological treatment in different solid organ tumors and also highly emetogenic chemotherapeutic use. Randomized, double-blind, placebo controlled future studies with more subject numbers are needed to understand properly the effect of acupuncture on CINV.

If classical antiemetic modality is not adequate to prevent nausea and vomiting, acupuncture is advised in addition to antiemetics as an effective method.

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