Laser Stimulation of Nei-guan Acupuncture Point as an Adjunct Modality to Conventional Antiemetics in Breast Cancer Patients

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ABSTRACT

Background: *Nausea and to a lesser extent vomiting remain significant clinical problems after the administration of chemotherapy, with up to 60 % of patients reporting nausea despite use of antiemetics. Combining antiemetics with other non- pharmacological treatment may prove to be more effective in decreasing nausea than antiemetics alone. The aim of the current study was to evaluate the effectiveness of using laser stimulation at pericardium 6 (neiguan – p6) acu-point in managing chemotherapy – induced nausea and vomiting.* ***Methods:*** *In this study (across matching controlled trials) the laser stimulation was applied bilaterally on P6 for five consecutive days after chemotherapy in ten patients who received chemotherapy. Another ten patients were standing as control group. On the second cycle of chemotherapy, the assigned of groups were reversed. The Rhodes Index of Nausea, Vomiting and Retching (INVR) was used daily to evaluate signs and symptoms for both groups throughout the study (five days).* ***Results:*** *It was found that nausea, vomiting, retching (experience, occurrence and distress) were all significantly lower in the studied group compared to the control group ($P<0.05$).* ***Conclusion:*** *Results highlight the important role of safe and convenient non- pharmacological complementary therapies such as laser stimulation in the management of the complex symptoms of chemotherapy- related nausea and vomiting.*

INTRODUCTION

Nausea, vomiting and retching (NVR) are among the most common and distressing symptoms that patients with cancer endure, both as a result of antineoplastic treatment and from the disease itself[8].

Nausea and vomiting are the most frequently reported adverse effects of antineoplastic chemotherapy and significantly affects patient's daily functioning quality of life, and compliance with therapy[4]. Effective management of these individual symptoms during initial and continued therapy profoundly influences symptom response throughout the cancer trajectory. Even mild NVR may have later sequelae e.g. anticipatory symptoms in patients receiving chemotherapy.

Vomiting results from an intricate succession of physiological events mediated by afferent innervations, humeral factors and somatic visceral musculature that are ultimately coordinated by the emetic or vomiting center located in the medulla. Afferent input to the emetic center originates

primarily from many sources. The cerebrocortical pathway which is stimulated by learned associations; the chemoreceptor trigger zone (CTZ) that is located in the area postrema in the cortex and is sensitive to chemical stimuli from the cerebrospinal fluid and blood; the vestibular pathway, which activates the emetic center via body positional changes (as in motion sickness); and the peripheral pathway, which is activated by neurotransmitter receptors found in the gastro intestinal tract where the vagus nerve communicates with emetic center[5].

Many different pharmacologic approaches have been investigated with varying degrees of success in an attempt to minimize NVR. However, concerns regarding the side effects associated with traditional antiemetics and the large cost of the newer drugs have increased interest in the use of non pharmacological techniques[15].

According to traditional Chinese medicine doctrines, illness results from an imbalance in the flow of energy through the body. This energy or Qi (chee) is restored with the use of acupuncture on certain points in the body which have been identified through critical observations and testing over 4000. In scientific terms, neurochemicals released after needling in a specific point may be responsible for relieving of nausea and vomiting in pericardium 6 (Nei-guan or P6) located above the wrist. Since the early studies has almost consistently shown that adding acupuncture to antiemetic therapy can significantly decrease nausea and vomiting[3].

Stimulation of P6 acupoint (Nei-Guan) may be a useful alternative to antiemetic drugs[17]. It is effective in the treatment of NVR. Unfortunately, the results of the published studies[7] regarding the effectiveness of this modality are inconclusive because of inadequate blinding of the patients, investigators or both, insufficient time of stimulation or poorly defined outcome measures. Therefore, the present double – blinded and cross matching study were designed to evaluate the effectiveness of using laser stimulation in pericardium 6 (Neiguan P6) acu-points in managing chemotherapy – induced nausea and vomiting.

SUBJECTS, MATERIAL AND METHODS

Subjects

Twenty highly educated female patients with mean age 51 ± 12.2 years had breast cancer were recruited from National Cancer Institute, Cairo University. All subjects were newly diagnosed and chemotherapy Naïve, starting their first cycle of chemotherapy. Inclusion criteria were a breast cancer diagnosis, stage of cancer 1-11, no prior experience of chemotherapy, receiving doxorubicin and cyclophosphamide or equivalent epirubicin protocols, and willing to sign a consent form .They were assigned randomly to one of the two groups (treatment or sham group). The revised Rhodes index of nausea, vomiting and retching (INVR) was used to collect the data .This is an eight item five point Likert – type self report pencil and paper instrument measuring the patient's perceived nausea, vomiting and retching experience, occurrence and distress reporting high reliability. Subjects were instructed to mark through or draw around the sentence in each raw what most clearly corresponds to their experience. Subscale scores can be calculated for nausea, vomiting and retching experience, occurrence and distress separately as well as for total experience, occurrence and distress. Scores for individual items can range from 0 to 4 with higher scores indicating more nausea, vomiting or retching.

0	strongly disagree
1	disagree
2	neither agree nor disagree
3	agree
4	strongly agree

Symptom occurrence refers to the frequency, duration and severity with which a symptom occurs. Where symptom distress, the degree of physical or mental upset, anguish or suffering experienced from the specific symptom. And symptom experience is the patient's perception of and response to the occurrence and distress of a symptom. In this index nausea is defined as unpleasant sensation experienced in the back of the throat and epigastrium that may or may not culminate in vomiting. It is synonymously described as feeling "sick at stomach".

Vomiting is the forceful expulsion of the contents of the stomach through the oral or nasal cavity. Where retching is the attempt to vomit without bringing any thing up.

Procedures

In this double – blind control study, each patient in the treatment group was received laser on Nei-guan acupuncture point (P6) which is located at the wrist between the tendons of the palmaris longus and flexor carpi radials, 2 cun proximal from the distal palmer crease. One cun is equivalent to the width of the patient's thumb across the interphalangeal joint (Fig. 1). Low level laser stimulation was used with the following characteristics; diode laser with continuous laser beam; power output 10 mw/cm^2, wave length 670 nm, laser (pointer laser device – petro - electric-Germany). Laser stimulation was performed on each P6 bilaterally over two minutes daily for five consecutive days after chemotherapy session. In control group, the same device was held on P6, but the laser beam was not activated. Neither the parents nor the investigators who stand for INVR evaluation were known if the laser was active. On the second cycle of chemotherapy, the assigned of groups were reversed. Another ten patients were received sham laser (as a control group). On the second cycle of chemotherapy, the assigned of groups were reversed.

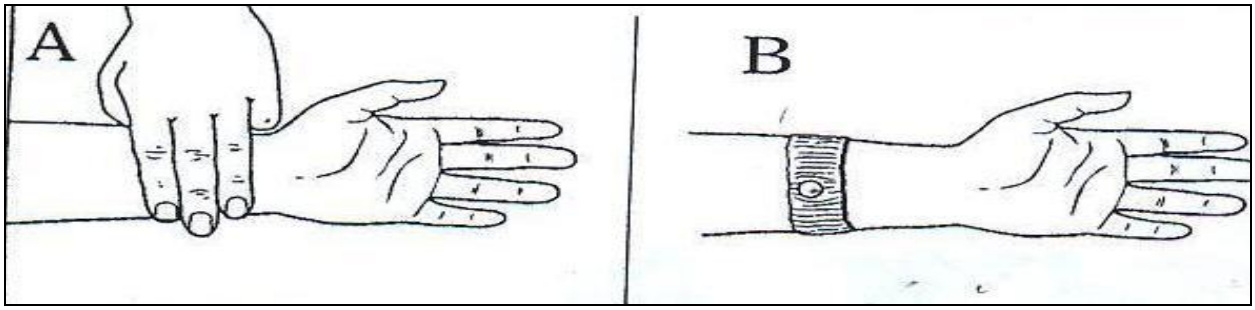

Fig. (1): Represents the point location above the wrist.

Data analysis

Data were coded and entered into SPSS (V.11) for statistical analysis. Descriptive statistics were calculated with all sociodemographic and clinical data and nausea, vomiting or retching subscale. Repeated measures analysis of variance was used to assess the levels of nausea, vomiting and retching between the two studied groups.

RESULTS

It was found that nausea was experienced significantly less often in the studied group compared to the control group P<0.001 across the five days of assessment. Only at day 3 both groups had similar levels of nausea. Similar results were observed with regards to retching experienced P=0.02. Vomiting experienced closely approached significance P=0.06. (Table 1).

Table (1): Descriptive statistics of nausea, vomiting and retching experience between the studied and control group [mean± (SD)].

		1st day	2nd day	3rd day	4th day	5th day
Nausea experience	Studied group	0.87 ±2.2	0.93 ±2	2.46 ±3.5	1.53 ±2.7	1.46 ±3.1
	Control group	2.72 ±3.1	2.94 ±2.9	2.55 ±2.9	3.22 ±3.4	2.5 ±3.4
Vomiting experience	Studied group	0.66 ±2.6	0.46 ±1.8	0.73 ±1.5	0.2 ±0.5	0
	Control group	0.94 ±2.75	0.66 ±2.2	0.66 ±2.2	0.6 ±1.9	0.5 ±1.54
Retching experience	Studied group	0.06 ±0.2	0.40 ±1.05	0.80 ±1.5	0.46 ±0.9	0.13 ±0.35
	Control group	0.50 ±1.7	0.78 ±1.8	0.66 ±1.5	0.78 ±1.7	0.50 ±1.3

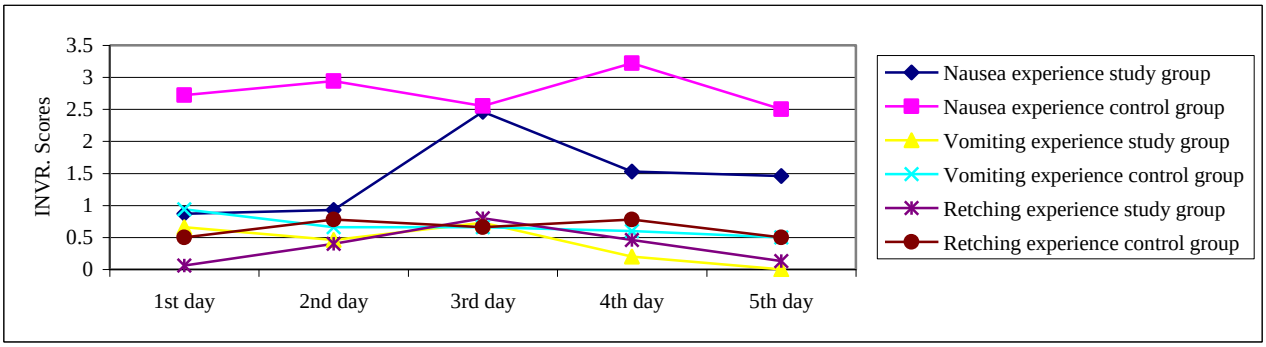

Fig. (2): Mean values of nausea, vomiting and retching experience scores after treatment in both groups.

Nausea, vomiting, and retching occurrence

Nausea occurred significantly less frequently in the studied group compared to the control group P<0.001 across the five assessment days. Day 3 had similar level of nausea occurrence in both groups. Significant improvement was found with regards to vomiting with days 4 and 5. Retching occurrence was also significantly lower in the studied group.

Table (2): shows descriptive statistics of nausea, vomiting and retching occurrence between the studied and control group [mean± (SD)].

		1st day	2nd day	3rd day	4th day	5th day
Nausea occurrence	Studied group	0.66 ±1.6	0.8 ±1.61	1.93 ±2.9	1.2 ±2.2	1.2 ±2.6
	Control group	2.16 ±2.4	2.27 ±2.1	2.05 ±2.4	2.55 ±2.5	1.94 ±2.3
Vomiting occurrence	Studied group	0.53 ±2.1	0.33 ±1.3	0.46 ±0.99	0.13 ±0.5	0
	Control group	0.66 ±1.94	0.39 ±1.2	0.44 ±1.5	0.39 ±1.2	0.22 ±0.6
Retching occurrence	Studied group	0.06 ±0.3	0.26 ±1.03	0.33 ±1.04	0.13 ±0.35	0
	Control group	0.17 ±0.7	0.38 ±0.8	0.39 ±0.8	0.5 ±1.04	0.22 ±0.5

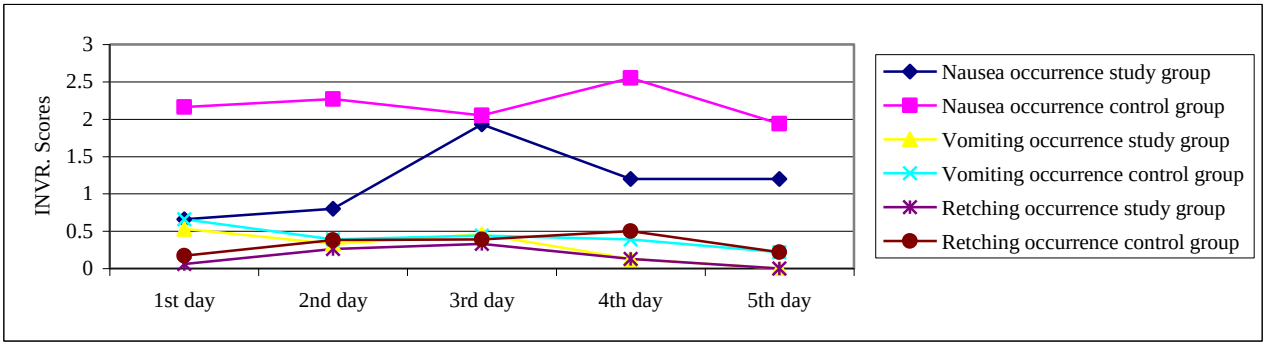

Fig. (3): Mean values of nausea, vomiting and retching occurrence scores after treatment in both groups.

Nausea, vomiting and retching distress

Both nausea and vomiting produced significantly less distress in the studied group than control group (P=0.002 and P=0.018) respectively, with day 3 of chemotherapy being similar in both groups. While distress from retching was significantly lower in the studied group (P=0.017, the control group had less distress than the studied group at day 3 and 4 as shown in table (3).

Table (3): Descriptive statistics of nausea, vomiting and retching distress between the studied and control group [mean ± (SD)].

		1st day	2nd day	3rd day	4th day	5th day
Nausea distress	Studied group	0.2 ±0.6	0.13 ±0.5	0.53 ±0.8	0.33 ±0.6	0.27 ±0.6
	Control group	0.55 ±1.04	0.67 ±0.9	0.5 ±0.8	0.57 ±0.9	0.55 ±1.1
Vomiting distress	Studied group	0.12 ±0.5	0.12 ±0.5	0.25 ±0.6	0.06 ±0.25	0.31 ±0.4
	Control group	0.28 ±0.8	0.28 ±0.95	0.22 ±0.7	0.22 ±0.7	0.67 ±0.9
Retching distress	Studied group	0.12 ±0.5	0.12 ±0.3	0.43 ±0.7	0.44 ±0.7	0.19 ±0.4
	Control group	0.33 ±1.02	0.39 ±0.9	0.28 ±0.75	0.28 ±0.75	0.28 ±0.95

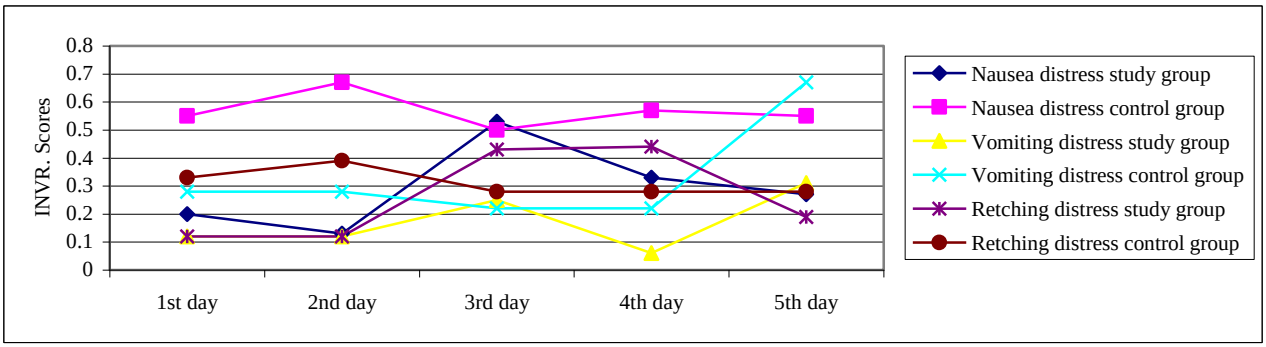

Fig. (4): Mean values of nausea, vomiting and retching distress scores after treatment in both groups.

DISCUSSION

Findings from the present study confirmed that chemotherapy–related nausea experience, occurrence and distress were significantly lower in the laser group than in the control group. This is in accordance with the accumulating body of evidence related to laser during chemotherapy and shows that laser is a safe and complementary option in the

management of chemotherapy- related nausea and vomiting[14].

A large number of studies have demonstrated that laser can relieve nausea and vomiting postoperatively[18] or after laparoscopy during pregnancy[16] and for motion sickness[2]. Furthermore a systematic review of 26 postoperative trials (N=3347) confirms that laser stimulation in general at point P6 significantly reduces the risk of nausea, vomiting and the need for rescue antiemetics[6]. Nevertheless negative studies do exist[1] but these are significantly outnumbered by the number of studies showing positive results. Also differences in the technique used and the use of sham laser may be responsible for such findings. Only a handful of such studies have been published using chemotherapy patients. An electronic search in MEDLINE, CINAHL and PubMed between 1990 and May 2005 using the search terms, laser and nausea or vomiting and chemotherapy or cancer revealed ten published studies. Seven of these studies showed positive findings and a further two studies closely approached statistical significance. Only one study showed negative results with a laser stimulation method. Among the studies showing significant (or the two close to the significance) reductions in chemotherapy-related nausea and vomiting, three trials used a Relief Band (a small battery- operated TENS device designed to stimulate the P6 acupoint) with samples from 18-50 patients[10], three used a Sea Band (an elastic wristband with a round plastic button applying pressure to P6 acupoint) using small samples [19] and two used direct pressure at the P6 acupoint[14] or a combination of P6 and ST36 acupoints. Roscoe et al. (2003)[11] using a large sample of 739 patients testing acupressure and acustimulation showed that men using acustimulation had less nausea and vomiting compared to the control group whilst women using acupressure wrist bands on the day of treatment had reductions closely approaching statistical significance. However, a recent randomized trial by Roscoe et al. (2005)[12] using acustimulation wrist bands showed no effects in controlling nausea and vomiting after chemotherapy in 96 breast cancer patients. Another negative study was also found but this was published in conference proceedings and used bone marrow transplant patients receiving high doses of chemotherapy, although details of the study were not available for assessment[9]. However, past studies are hampered by the different types of antiemetics used, differences in the risk factors of nausea and vomiting, the chemotherapy regimen used and sampling issues. Also, although most studies were randomized trials, some used crossover or observational designs.

A puzzling finding was the high level of nausea, retching and vomiting at day 3 in the laser group, equal to the experienced by the control group. This finding has been reported elsewhere too[11]. This may be related to G1 disturbance associated with use of dexamethasone or more remotely because of constipation secondary to granisetron. Indeed the latter was something communicated to us by a couple of women in the study in follow up appointments. It may also be that day 3 in the peak of nausea and vomiting related to the types of chemotherapy given to the study's subjects, a day difficult to manage with complementary techniques only. As women in the study were prescribed antiemetics on a PRN basis, many may have stopped using them or relaxed their use being already a couple of days post chemotherapy with low levels of nausea and vomiting the previous two days. It would be interesting to see whether use of antiemetics at 3rd day at regular intervals combined with laser would lead to

different results, or whether the outcome of laser acupuncture is affected by the presence of side effects from antiemetics used. It does show, however, that 3rd day post-chemotherapy is a day deserves more attention in terms of antiemetics management. However, findings should be viewed in light of the study's limitations, including a small sample size due to funding constraints. Furthermore, although antiemetics given before chemotherapy were standardized antiemetics for days 2-5 were not controlled, as there is no standard clinical practice (despite the availability of clinical antiemetic guidelines) and controlling for such use would have been unethical and would have conflicted with the experience of the physicians. The influence of anticipatory symptoms in the development of post- chemotherapy nausea and vomiting was also not accounted for the present study.

Laser acupuncture seems to be a good way to complement antiemetic pharmacotherapy, as it is safe, convenient and with minimal costs. It is not known why acupuncture works, and partly these results may be attributed to a placebo effect as also highlighted in the study by Roscoe et al. (2003)[11]. The mechanism whereby P6 acupressure reduces symptoms of motion sickness is still unknown. Researchers have suggested that laser acupuncture increases endorphin levels and adjustment of autonomic nerves[20].

Conclusion

The antiemetic effects of P6 stimulation by a low level laser were similar to those reported in studies which investigated the effects of antiemetic agents in children undergoing strabismus surgery. Therapy with drugs such as ondansetron, droperidol and metoclopramide, however, is often associated with side effects. In comparison, stimulation of P6 with a low level laser has no known side effects. However, it must be recommended that direct laser irradiation of the retina should be avoided by laser- protection glasses and correct handling.

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الملخص العربي

استخدام الليزر في تحفيز نقطة الوخز بالإبر كوسيلة مساعدة لمضادات القيء التقليدية لمرضى سرطان الثدي

الغثيان والقيء تعتبر من المشاكل الهامة التي تصاحب العلاج الكيميائي لمرضى سرطان الثدي بنسبة تصل إلى حوالي 60% على الرغم من استخدام مضادات القيء التقليدية. لذلك كان الهدف من هذه الدراسة هو تقييم تأثير استخدام الليزر على نقطة الوخز بالإبر لتقليل نسبة الغثيان و القيء . أجريت الدراسة على عشرين مريضا لمدة خمسة أيام بعد استخدام العلاج الكيميائي وتم تقييم الأعراض خلال فترة هذه الدراسة . أظهرت النتائج حدوث تحسن ملحوظ ذو دلالة إحصائية في المجموعة التجريبية مقارنة بالمجموعة الضابطة و ذلك يعكس أهمية استخدام الليزر لهذه الحالات إلى جانب العلاج التقليدي للغثيان والقيء بعد العلاج الكيميائي لمرضى سرطان الثدي .