Effect of TENS and P6 Accustimulation on Chemotherapy Induced Nausea and Vomiting in Postmenopausal Women

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ABSTRACT

Background: *Nausea, vomiting and retching were significant clinical problems accompanied with administration of chemotherapy, up to 60% of patients reporting nausea despite use of antiemetics. Non-pharmacologic techniques may be effective in reducing nausea, vomiting and retching.* ***Purpose of the study:*** *to investigate the effect of transcutaneous electrical nerve stimulation (TENS) and acupressure at P6 (Neiguan point) in reducing nausea, vomiting and retching induced by chemotherapy.* ***Methodology:*** *30 postmenopausal breast cancer women treated by chemotherapy participated in this study and randomly assigned into 2 groups, group (A) received TENS and acupressure at P6 for 5 days, while group (B) received placebo treatment.* ***Assessments*** *of nausea, vomiting and retching were collected from all patients daily for 5 days and measured by the revised Rhodes Index of Nausea, Vomiting and Retching (INVR).* ***Results:*** *Nausea, vomiting and retching occurrence were significantly reduced in the study group compared to the control group ($P<0.05$).* ***Conclusion:*** *this study suggested that the combination of TENS and acupressure at P6 plus antiemetics have a good effect to prolong the reduction of chemotherapy induced nausea, vomiting and retching.*

Key words: *cancer, chemotherapy, vomiting, TENS, acupressure.*

INTRODUCTION

Nausea and vomiting are basic human protective reflexes against the absorption of toxins, as well as responses to certain stimuli. They are often used together, although each phenomenon should be assessed separately[29].

Nausea is defined as a subjectively unpleasant wavelike sensation in the back of the throat or epigastrium associated with pallor or flushing, tachycardia, and an awareness of the urge to vomit. Sweating, excess salivation, and a sensation of being cold or hot may occur. Vomiting, or emesis, is characterized by contraction of the abdominal muscles, descent of the diaphragm, and opening of the gastric cardia, resulting in forceful expulsion of stomach contents from the mouth[5].

Nausea of varying intensity is a very common side-effect of chemotherapy. Chemotherapeutic agents stimulate enterochromaffin cells in the gastrointestinal tract to release serotonin, which activates serotonin receptors. Activation of these receptors activates the vagal afferent pathway, which activates the vomiting center and causes an emetic response[6].

Chemotherapeutic agents are rated according to their emetic potential;[1] indicates the least potential, and the organization of ASHP, (1999)[5] indicated the greatest. The

American Society of Health System Pharmacists recommends prophylactic antiemetic therapy when drugs with antiemetic potential of levels 2 to 5 are used.

In addition to the emetic potential of the chemotherapeutic agents, several other risk factors can be used to predict the likelihood of chemotherapy-induced nausea and vomiting (CINV). Such as Patients younger than 50 years, women are more susceptible because of the influence of hormones, a history of motion sickness, pregnancy-related nausea and vomiting, or nausea and vomiting with previous chemotherapy are all positive predictors of CINV[29,33].

Acupuncture is a scientifically accepted method for treating pain. It has also been shown to reduce nausea effectively in seasickness and morning sickness during pregnancy, as well as in patients pre-medicated with opioids before surgery[23].

Mayer, 2000[23], found that acupuncture administered at point P6 (Neiguan) significantly improved nausea in 97% of the 130 cancer patients studied. This effect was absent when a placebo point was tested.

Transcutanous electrical nerve stimulation (TENS) has traditionally been used for the treatment of pain, in addition, decrease the frequency and severity of some types of nausea and vomiting. A TENS device consists of an electronic stimulus generator that transmits pulses of electrical current to electrodes on the skin. TENS is closely related to the techniques of acupressure and acupuncture from traditional Chinese medicine. This tradition is based on the concept that stimulation of specific body points can restore a state of normal balance and relieve symptoms of illness. One of these specific points is designated for antiemetic treatment[8].

SUBJECTS, MATERIALS AND METHODS

30 newly diagnosed breast cancer postmenopausal women were included in the study from National Cancer Institute (NCI), Cairo University. Their ages ranged from 50-60 years and diagnosed as breast cancer that was being treated with chemotherapy included (cyclophosphamide, 5Fu, and Adriamycin). A written consent form was signed from all participants before treatment, and scheduled to receive their first course of chemotherapy. Patients had to have a predicted life expectancy of ≥4 months. Then a randomized classification of patients was done to form 2 groups, all participants in both groups received standard antiemetics before chemotherapy with Zofran 8 mg as a prophylactic for acute nausea and vomiting.

Group (A) treatment group: consisted of 15 patients received a 30 minutes of TENS (frequency 10-15 Hz at P6 and the reference electrode was applied at the thenar muscles) before starting chemotherapy. Then, it was applied for 20 minutes/day with continues application of accu-band on the same stimulated P6 points and pressing the button for 5 minutes every 2 hours in the patients dominant side while she awake for 5 days in addition to antiemetics drugs when necessary to overcome both acute and delayed episodes of nausea and vomiting. P6 is located (on the anterior surface of the forearm, 5 cm proximal to the distal wrist crease, between the tendons of the flexor carpiradialis and the palmaris longus) applied in the patient's dominant side to overcome both acute and delayed episodes of nausea and vomiting.

Group (B) control group: consisted of 15 patients, they had given antiemetics drugs when necessary with unbearable episodes of nausea and vomiting in addition to placebo

TENS and accu-band on the dorsum of the wrist joint with the same schedule as group (A).

All patients were assessed by the revised Rhodes Index of Nausea, Vomiting and Retching occurrence[26] which were completed every evening after the chemotherapy administration and for five successive evenings. Outcome criteria were nausea, vomiting and retching occurrence on a 4-point scale (none = 0, mild = 1, moderate = 2, severe = 3).

Data analysis

Descriptive statistics were calculated with clinical data, and nausea, vomiting or retching subscale scores. Repeated measures analysis of variance (R-ANOVA) was used to assess the levels of nausea, vomiting and retching between the two study groups.

RESULTS

TENS and acupressure significantly reduced the severity, duration of nausea, retching as well as the bouts number of vomiting from the first to fifth day.

Nausea decreased significantly ($P<0.001$) in group A than group B across the five assessment days (table 1 and fig. 1).

Vomiting occurrence showed significant improvement ($P<0.05$), mostly in fourth and fifth days in group A than group B (table 2 and fig. 2).

The retching occurrence was also highly significant decreased ($P < 0.034$) in group A than group B, (table 3 and fig. 3).

The total nausea, vomiting and retching occurrence were also highly significant decreased in group A ($P < 0.001$) compared with group B.

Table (1): Shows the nausea occurrence in both groups (A and B).

Variable	Groups	1st day	2nd day	3rd day	4th day	5th day
Nausea occurrence	Group (A)	0.57±1.4	0.69±1.41	1.09±2.54	1.04±1.93	1.04±2.28
	Group (B)	1.69±1.88	1.78±1.64	1.60±1.88	2.00±1.96	1.52±1.80

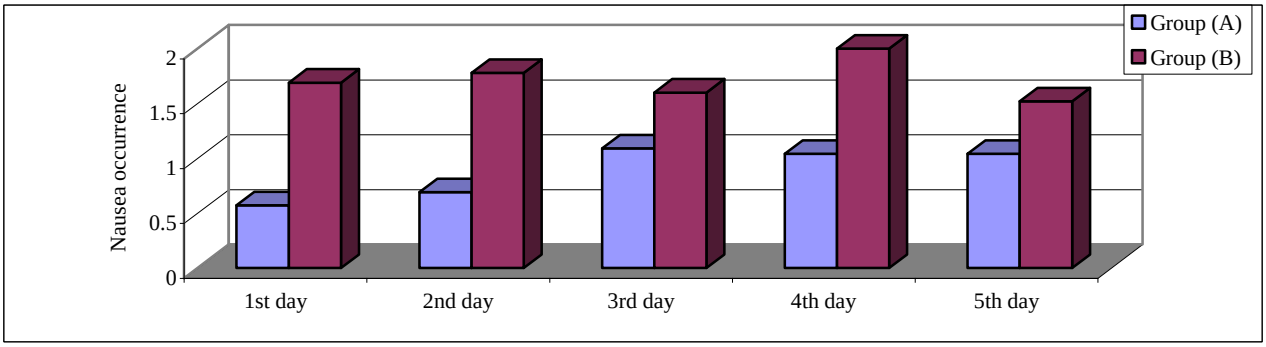

Fig. (1): Shows the nausea occurrence in both groups (A and B).

Table (2): Shows the vomiting occurrence in both groups (A and B).

Variable	Groups	1st day	2nd day	3rd day	4th day	5th day
Vomiting occurrence	Group (A)	0.45±1.84	0.28±1.13	0.39±0.86	0.10±0.43	0
	Group (B)	0.51±1.52	0.29±0.93	0.33±1.17	0.29±0.93	0.16±0.46

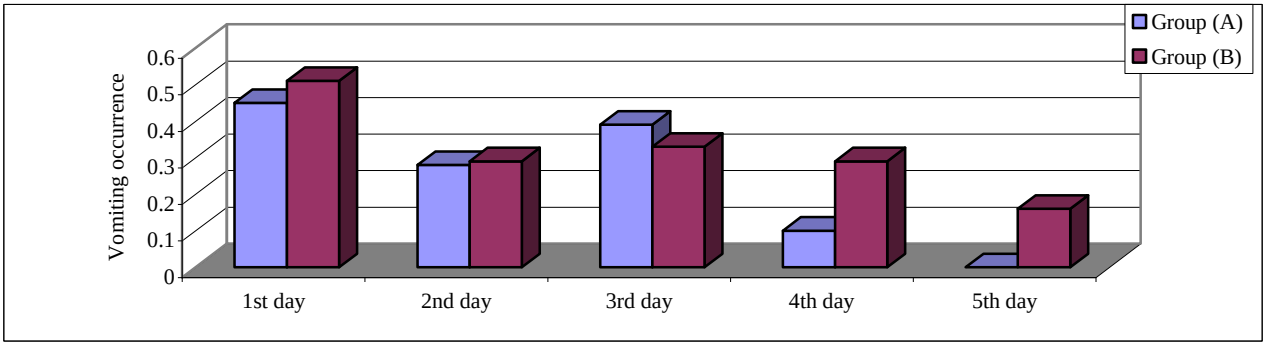

Fig. (2): Shows the vomiting occurrence in both groups (A and B).

Table (3): Shows the Retching occurrence in both groups (A and B).

Variable	Groups	1st day	2nd day	3rd day	4th day	5th day
Retching occurrence	Group (A)	0.04±0.25	0.21±0.89	0.28±0.90	0.10±0.29	0
	Group (B)	0.12±0.54	0.20±0.62	0.29±0.62	0.38±0.81	0.16±0.38

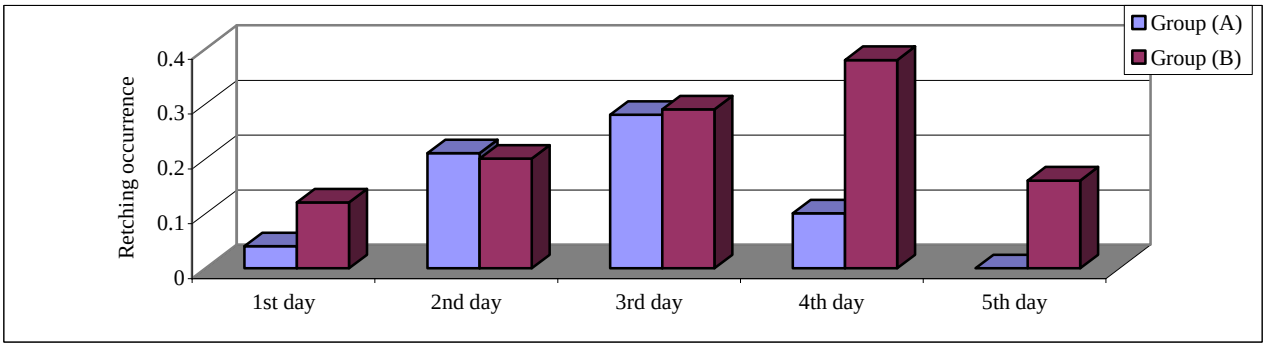

Fig. (3): Shows the retching occurrence in both groups (A and B).

DISCUSSION

Non-pharmacological methods like acupuncture, acupressure and laser stimulation have shown comparable antiemetic efficacy. The P6 (Nei-Guan) point has been used to treat vomiting and other stomach disorders in traditional Chinese medical practice[12,30].

The results from the present study confirmed that chemotherapy related nausea, retching and vomiting were significantly lowered in the study group (A) than placebo or control group (B). Nausea and retching were highly significant decreased ($P < 0.001$ & 0.034) respectively, while vomiting was significantly lowered ($P < 0.05$) in the study group compared to the control group. It is due to the accumulating body of evidence related to TENS and acupressure which are a safe and complementary option in the management of chemotherapy related to nausea and vomiting.

The nausea, vomiting and retching occurrence were high in both groups on the third day because due to chemotherapy induction. Also, it may be due to gastrointestinal disturbance associated with the use of dexamethasone. Its incidence in the control group may be due to the previously mentioned causes in addition to many patients may stopped using the antiemetics or relaxed

their use being already a couple of days post chemotherapy with low levels of nausea, retching and vomiting. So, we can conclude that the third day post chemotherapy may need more attention by increasing the TENS application frequency in the study group and to be sure that the patients taking the exact dose of antiemetics or increase it in the control group.

The mechanism of action is postulated that acupressure causes low frequency electrical stimulation of the skin sensory receptors which may activate A ß and A δ fibers. These fibers synapse within the dorsal horn and may, in turn, cause release of endorphins from the hypothalamus. Increased levels of ß-endorphin concentration have been reported in human cerebrospinal fluid after acupuncture stimulation and ß-endorphins may have antiemetic effects mediated by its action on μ receptors[10].

In addition, serotonergic and norepinerphrinergic fibres may be activated and a possible change in serotonin levels has a role in prevention of post operative nausea and vomiting (PONV). Acupressure has been shown to enhance gastric motility[22]. There is also a possible role of central dopaminergic receptors in acupuncture. The antiemetic effect of the P6 point may be mediated by an action opposing to that of central dopamine[19].

Electro-acupuncture (repeated sensory stimulation) has been thought to modulate serotonin, substance P, and endogenous opiates along various pathways in the central nervous system. Some effects may be manifested through the serotonin- and substance P–mediated components of the emetic reflex, as well as through the opiate μ receptor via its antiemetic actions[7,27].

The mechanisms of acupuncture on nausea and vomiting are largely unknown. Acupuncture may affect the sympathetic system via mechanisms at the hypothalamic and brainstem levels. The hypothalamic beta-endorphinergic system exerts inhibitory effects on the vasomotor centre. There is evidence that hypothalamic nuclei have a central role in the mediating effects of acupuncture and that afferent input of somatic nerve fibres has a significant effect on autonomic functions[4].

Dibble et al. (2007)[11], compared the differences in the chemotherapy-induced nausea and vomiting (CINV) among three groups of women (acupressure, placebo acupressure, and usual care) undergoing chemo-therapy for breast cancer, and concluded that Acupressure at the P6 point is a safe and effective tool in addition to pharmaceutical management for managing delayed CINV and should be offered to women undergoing chemotherapy for breast cancer[11].

TENS at P6 has been widely investigated and concluded a significant reduction in chemotherapy induced nausea and vomiting in pediatric tonsillectomy[28], pediatric oncology[18] and adult oncology[25,3,9].

Self-administered acupressure appears to have a protective effect for acute nausea and can readily be taught to patients. Noninvasive electro stimulation at P6 appears unlikely to have a clinically relevant impact when patients are given state-of-the-art pharmacologic antiemetic therapy[17].

The pioneering work on the use of acupuncture for chemotherapy-induced nausea and vomiting, as well as for postoperative nausea and vomiting and morning sickness, was performed by Dundee et al. (1988), involved 24 inpatients receiving various chemotherapy regimens. All patients had experienced severe sickness (nausea and/or vomiting) with a prior infusion of chemotherapy. The patients received 5 or 6 treatments over 3 days with electro

acupuncture (10 Hz, 5 minutes) of PC 6 (right forearm only), the first treatment being given prior to administration of chemotherapy. Eleven inpatients and 21 outpatients had complete alleviation of emetic symptoms lasting at least 8 hours following treatment with acupuncture while most of the remaining patients had some improvement. Sham acupuncture using a point near the right elbow was without benefit[15].

Gan et al. (2004)[20] investigated the effect of electro-acupuncture compared with ondansetron 4 mg and placebo in women undergoing major breast surgery. Electrical stimulation was applied 30-60 min before induction of anesthesia and continued until the end of surgery. There was a clear effect of both active groups; the complete response rate (no nausea, vomiting, or rescue medication) was greater in the acupuncture (73%) and ondansetron groups (52%) at 24 h post operative compared with placebo (38%). The incidence of nausea at 2 h post operative was significantly less in the acupuncture group (19%) compared with the ondansetron (40%) and placebo group (79%)[20].

McMillan et al. (1991)[24], assessed the effect of transcutaneous electrical stimulation (TCES) as an adjunct to ondansetron for relief of nausea and vomiting in 16 patients receiving a chemotherapy regimen. TCES of 10-15 Hz for 5 minutes every 2 hours awake for 5 days, was applied to PC 6 (negative pole) and LI 4 (positive pole) on the patients' dominant forearm. The severity of nausea and the incidence of vomiting were reduced by TCES treatments in 12 patients[24].

Dundee et al. (1991)[16], investigated that if acupressure could prolong the antiemetic effect of TCES. Unilateral PC 6 acupressure applied following TCES prolonged the antiemetic effect for 24 hours in approximately 90% of patients. Despite of previous studies concluded that unilateral acupressure treatment alone was ineffective for relieving chemotherapy-induced nausea and vomiting, but appears to help prolong the antiemetic effect of PC 6 acupuncture and TCES to relief of chemotherapy-induced nausea and vomiting[16].

Acupressure was investigated in post-operative nausea and vomiting (PONV) after laparoscopic cholecystectomy. Wristbands applied 30 min before surgery at P6 were compared with placebo and ondansetron 4 mg. and revealed a significant decrease of PONV after surgery; in the first 6 h (when the wristbands were applied) in comparison to ondansetron 4 mg and placebo while there were similar in their effect in the rest of 24 h post-operative[1].

Zarate et al. (2001)[34], investigated the efficacy of acustimulation for PONV which was applied 10 min before the end of surgery and remained in situ for 9 h as active, sham relief band at P6 and sham relief band on the dorsum of the wrist, There was a significantly decreased incidence of moderate-severe nausea for up to 9 h after surgery in the active treatment group compared with the sham and placebo groups. However, there were no differences in the incidence of vomiting[34].

While the combination of accustimulation (Relief Band for 72 h) with ondansetron 4 mg in 120 patients undergoing plastic surgery. This combination significantly reduced the incidence of nausea (20 versus 50%), vomiting (nil versus 20%) and need for rescue analgesia (10 versus 37%). Also, the ability to resume a normal diet within 24 h, quality of recovery, and patient satisfaction were significantly superior in the combined group, but statistical significance was not reached. They concluded that acustimulation had a prophylactic antiemetic effect[32].

Accustimulation with the Relief Band was most effective in reducing postoperative nausea and vomiting and improving patients' satisfaction with their antiemetic therapy when it was administered after surgery[31].

Dundee et al. (1989)[14], noted that a single acupuncture treatment of PC 6 was an effective adjuvant to standard antiemetic therapy in cancer chemotherapy, but the benefit lasted only 8 hours. Dundee and Yang, (1990)[13], placed an acupuncture wristband (unilateral) on PC 6 immediately following PC 6 acupuncture (unilateral, dominant forearm, 10 Hz, 5 minutes) and instructed patients to press the button for 5 minutes every 2 hours while awake until 24 hours following chemotherapy. In 40 patients, use of acupressure prolonged the antiemetic effect of acupuncture for 24 hours following 95% of the treatments[14].

In contrast, when wristbands applied at the P6 point for 30 minutes before different urologic surgeries and removed 6 hours post operative have been compared with placebo in 200 patients. 25% of the acupressure group experienced PONV compared with 29% of the placebo group (not significant)[2].

Also, Habib et al. (2006)[21], randomized 94 patients undergoing cesarean delivery with spinal anesthesia to receive transcutaneous acupoint electrical stimulation using the Relief Band at the P6 point (active group) or an active Relief Band applied to the dorsum of the wrist (sham control group). The Relief Band was applied 30-60 min preoperatively and left in place for 24 h. There was no statistically significant difference between the active and sham control groups in the incidence of intra-operative/postoperative nausea, vomiting, and need for rescue antiemetics[21].

In conclusion, from the obtained results, Accustimulation of P6 seemed to be an effective method in reducing nausea, vomiting and retching in addition to decrease antiemetics drugs in case of chemotherapy treatment for breast cancer in postmenopausal women.

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الملخص العربي

تأثير التيار المنبه للعصب عبر الجلد والتنبيه الأبري على الغثيان والقيء المصاحبان للعلاج الكيميائي في السيدات بعد انقطاع الدورة الشهرية

يعتبر الغثيان والتقيؤ من المشكلات الأكثر شيوعا بعد العلاج الكيمائي والذي تصل نسبة حدوثه إلى 60% من المرضي بالرغم من استخدام مضادات القيء وبالتالي كان الهدف من هذه الدراسة هو معرفة تأثير التيار المنبه للعصب عبر الجلد والضغط الابري عند نقطة مضاد القيء . وقد اشتركت في تلك الدراسة 30 سيدة في سن ما بعد انقطاع الدورة الشهرية يعانين من سرطان الثدي يعالجن بالعلاج الكيميائي و قد قسمن عشوائيا إلى مجموعتين متساويتين . المجموعة (أ) مجموعة الدراسة خضعن إلى التيار المنبه للعصب عبر الجلد والضغط الابري عند نقطة مضاد القيء لمدة 5 أيام متتالية بينما المجموعة (ب) المجموعة الضابطة خضعن إلى مضادات القيء إلى جانب العلاج الايحائي للتيار التنسي والوخز الايحائي . وقد قيمت درجة الغثيان والقيء عن طريق رودس اندكس وقد أظهرت النتائج انخفاض ذو دلالة إحصائية عالية في درجة الغثيان والقيء في مجموعة الدراسة بالمقارنة مع المجموعة الضابطة ومن ذلك نستطيع أن نستنتج أن الجمع بن التيار المنبه للعصب عبر الجلد والضغط الابري لتنبيه نقطة مضاد القيء يأتي بنتائج جيدة وملموسة لتخفيض درجة الغثيان والقيء الناتج عن العلاج الكيميائي .

الكلمات الدالة : السرطان- القيء- التيار المنبه للعصب عبر الجلد - الضغط الابري .