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Acupressure for Chemotherapy Induced Nausea and Vomiting in Breast-Cancer Patients: A Randomized, Placebo-Controlled Clinical Trial

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Abstract

Introduction: Chemotherapy is an important treatment in cancer (CA) care and is associated with numerous side effects. Early studies reported that patients cited nausea and vomiting as the most distressing symptoms when receiving chemotherapy. Despite continuing improvements in antiemetic therapies, nausea and vomiting following chemotherapy treatment for CA remains a significant clinical problem for many patients and there is correlation between the intensity of anticipatory nausea in the clinic prior to their treatment infusion and subsequent post treatment of nausea and vomiting.

Since pharmacological treatments have failed to completely manage nausea and vomiting, exploring the complementary, non-pharmacological, approaches that can be used in addition to pharmacological approaches becomes paramount. Acupressure at the P6 point is a value-added technique in addition to pharmaceutics; management for women undergoing treatment for breast cancer to reduce the incidence and intensity of delayed chemotherapy induced nausea and vomiting (CINV), since up to 60% of patients had been reported nausea despite the use of antiemetics **Aims:** The first aim is to examine the efficacy of P6-acupressure in preventing chemotherapy induced nausea and emesis associated with highly emetogenic chemotherapy (i.e. doxorubicin as adjuncts to standard 5-HT_3 antiemetics (granisetron) and dexamethasone antiemetic given as part of routine care in reducing acute nausea (during the day of treatment) and delayed nausea (2-5 days) following the day of chemotherapy. The second aim is to examine the efficacy of the acupressure bands in reducing vomiting and in maintaining Quality of Life (QOL). **Patients and methods:** A randomised, double-blind, placebo controlled trial. One group received acupressure with bilateral stimulation of P6 (n=42), a second group received bilateral placebo stimulation, (n=42) and a third group received no acupressure wrist band and served as a control group, (n=42). Acupressure was applied using a Sea-Band (Sea- Band UK Ltd., Leicestershire, England) which had to wear for the 5 days following the chemotherapy administration. Assessments of acute and delayed nausea and emesis, OOL, patients' satisfaction, recommendation of treatment and requirement of rescue antiemetic were obtained. **Results:** No significant differences were found in the incidence of acute nausea or emesis 24- h following chemotherapy by treatment groups. Significant difference was found in the severity of early nausea (0-6 scale) in the acupressure group M (SD) 1.62 (2.04) as compared to placebo group 2.17 (2.09), p=, 0006.

The acupressure group had a statistically significant reduction in the incidence of delayed nausea 40% (17/42) as compared to the control group 62% (26/42) (p= ,0495). Further analyses indicated that significant difference existed in the intensity of delayed nausea by acupressure group mean (SD) 1.45 (1.73), p=, 0002 as compared to control 2.03 (1.91). Significant difference also existed in the intensity of delayed nausea by placebo group 1.33 (1.66), p=, 0010 as compared to control 2.03 (1.91). Here we noted a placebo effect.

The percentage of the patients who had delayed moderate to very severe nausea day 2-5 (≥3 on 0-6 scale) in the acupressure group is 55% (23/42 (p= 0206), in the placebo group 52% (22/42) (p= 0116), a statistically significant reduction existed as compared to control 79% (33/42). Here we noted a placebo effect.

The incidence of delayed vomiting episodes day 2-5 was 48% (20/42), 64% (27/42), and 57% (24/42) in the acupressure, placebo and control group respectively. No significant differences were found between the groups.

The mean of number of delayed emetic episodes day 2-5 was significantly less in the acupressure group 2.7 (1.87) as compared to placebo 3.3 (1.91), p=,0022 and control groups 2.07(1.20), P= ,0005. Requirement of rescue antiemetic was significantly lower in P6-acupressure (55%, 23/42), as compared to control group (76%, 32/42) (p= 0389).

81% (35/42)) of the patients in acupressure group were significantly satisfied with P6-acupressure as compared to placebo group 64% (27/42), p= 0.0471. 79% (34/42)) of the patients in acupressure group would

recommend P6-acupressure to another patients as compared to placebo group 62% (26/42), p= 0,0533 .

No statistically significant differences between groups were observed for the overall items response rate of the FACT-Scale which were 74/108, 67/108, 69/108 in the acupressure, placebo and control group respectively. **Conclusion**: P-6 Acupressure is efficacious for control of delayed chemotherapy related nausea and emesis and is a value-added method in addition to pharmaceutical management for women undergoing treatment for breast cancer. Placebo effect of acupressure decreased severity of delayed nausea day 2-5 but the mean of number of delayed emetic episodes and need of rescue antiemetics were reduced only by acupressure with the correct P6 point stimulation.
Keywords: breast cancer, chemotherapy, nausea, vomiting, acupressure.

1. Introduction

Cancer (Ca) is a group of diseases characterized by uncontrolled and growth spread of abnormal cells. It may be caused by internal factors (inherited mutation, hormonal, immune, conditions and mutation from metabolism) or external ones (tobacco, radiation, chemicals and infectious organisms). Cancer is prevalent all over the world among developed and developing nations; it affects both sexes at all ages. Breast cancer is the first leading cause of death of female cancers. Over 175,000 women in the US are diagnosed with breast cancer each year, the prevalence rising up to 7% over age 70 in the near future (LouWman et al, 2007). It occupies the first of female's CA among the Palestinians with incidence (15.1%) per 100,000 population, and mortality rate (5.2 %) per 100,000 females (MOH report 2005). CA treatment is based on chemotherapy, radiotherapy and surgical interventions. Radiotherapy is not available in the Palestinian territories, but the other two types are accessible at most governmental health settings at Gaza Strip and West Bank (WB) (MOH report 2005).

Chemotherapy is an important treatment in cancer care and is associated with numerous side effects such as bone marrow suppression, increased susceptibility to infection, nephrotoxicity, anorexia, alopecia, diarrhea, nausea and vomiting (Vincent et al, 2001). Early studies reported that patients cited nausea and vomiting as the most distressing symptoms when receiving chemotherapy (Coates et al 1983, Deboer- Dennert et al 1997). Beyond their distressing effects, severe nausea and vomiting can lead to nutritional deficiencies, dehydration and electrolyte imbalance and fatigue (Hawthorn 1995, Joss et al 1990, king 1997). Despite continuing improvements in antiemetic therapies, nausea and vomiting following chemotherapy treatment for CA remains a significant clinical problem for many patients and there is correlation between the intensity of anticipatory nausea in the clinic prior to their treatment infusion and subsequent post treatment nausea during the 24 h after the infusion (Bovbjer 2006).

Historically, antiemetic treatment has been improved first by the introduction in 1981 of high-dose metoclopramide which reduced the amount of emesis (Gralla et al 1981), second by the development of serotonin (5-HT3) antagonist in the early 1990s, potentiated by concomitant use of corticosteroids which further improved control of emesis (Grunberg, & Kesketh 1993). Despite these improvements, nausea and vomiting remain a problem for patients (Grunberg et al 2004). Recently a new drug, the neurokinin NK (1) receptor antagonist has been shown to have a better effect on preventing both acute and delayed CINV for patients treated with highly emetogenic chemotherapy (Dando & Perry 2004, Dewit et al 2004). Non-pharmacological interventions such as music (Ezzone et al 1998), acupressure (Dibbel et al 2000) and progressive muscle relaxation (Molassiotis et al 2002) have also been shown to reduce CINV.

The 5-HT_3 antagonists, are more effective than prior medications in preventing chemotherapy induced vomiting (DeMulder 1990, Marty 1990, Roscoe et al 2000, Osoba et al 1997). However, chemotherapy related nausea is not as well controlled by these drugs and remains a significant problem (Roscoe et al 2000). Uncontrolled nausea and vomiting (NV) can interfere with adherence to treatment regimens, and may cause oncologists to reduce chemotherapy doses (Morrow and Dobkin 1988, Stewart 1990). Nausea and vomiting can also disrupt the activities of daily living, because lost time from work, increase anxiety and depression, (king 1997)

In one study involving 1,413 cancer patients undergoing chemotherapy, 80% experienced nausea to some degree, with 40% having at least one episode of vomiting (Roscoe et al 2000). Similarly, in a study, 76% of 322 patients who received chemotherapy regimens containing cisplatin, carboplatin, or doxorubicin experienced nausea following their first treatment, despite what was felt by physicians to be adequate antiemetic prophylaxis. Of these 322 patients, 147(46%) had nausea of moderate severity or greater (Hickok et al 2003). Identifying methods to successfully prevent and alleviate treatment-related nausea remains a major clinical challenge.

Since pharmacological treatments have failed to completely manage nausea and vomiting, exploring the complementary role of other, non-pharmacological, approaches that can be used in addition to pharmacological approaches becomes paramount. Acupressure at the P6 point is a value-added technique in addition to pharmaceutics; management for women undergoing treatment for breast cancer to reduce the amount and intensity of delayed CINV, since up to 60% of patients had been reported nausea despite the use of antiemetics

(Dibble et al 2007).

Stimulation of the P6 acupuncture point located on the inside of the wrist with needles (acupuncture) or pressure (acupressure) has been used to relieve NV in traditional Chinese medicine for centuries (Beinfield and Korngold 1995). Literature reviews indicate that acupuncture and acupressure may provide relief from these symptoms (Kaptchuk 2002, Mayer 2000, Vickers 1996). Specifically, needling or applying pressure (generally with an acupressure band such as the SeaBand®, (Sea Band UK Ltd., Leicestershire, England) to an acupoint have been efficacious in alleviating morning sickness (Belluomini et al 1994, Carlsson et al 2000, DeAloysio and Penacchioni 1992, Norheim et al 2001, Evans et al 1993, Slotnick 2001), motion sickness (Hu 1992, 1995, Bertolucci and DiDario 1995, Stern et al 2001, Alkaissi 2005), post-surgical nausea (Fan et al 1997, Ferrara-Love et al 1996, Gieron et al 1993, Harmon et al 2000, Ho et al 1996, Stein et al 1997, Alkaissi 1999, 2002, Zarate et al 2001) and NV associated with chemotherapy (Dundee 1989,1991, Roscoe 2002, 2003, Shen et al 2000, Dibble 2000, Williams et al1992, Treish et al 2002, Bushunow et al 2002, Dundee and Yang 1990, Stannard 1989, Pearl et al1999, Noga et al 2002).

Beginning in the early 1990s, studies assessing the efficacy of electrical stimulation (acustimulation) using portable Transcutaneous Electrical Nerve Stimulator (TENS) wrist bands to the P6 acupuncture point for control of nausea have also been conducted. All of these studies used the Relief Band (Woodside Biomedical, Carlsbad, CA), which is marketed for this purpose and has United States Food and Drug Administration (FDA) clearance as treatment for NV. In 1998, the National Institutes of Health Consensus Statement on Acupuncture concluded that promising results have emerged showing the efficacy of acupuncture in adult postoperative and chemotherapy induced nausea and vomiting. The acupuncture point, P6 had been the point used in most of the trials (Ezzo et al 2006).

Acupressure seems to be a good way to complement anti emetic pharmacotherapy, as it is safe, convenient and with minimal costs involved. These make it a cost-effective intervention. It is not known why acupressure works, and partly these results may be attributed to a placebo effect, as also highlighted in the study by (Roscoe et al 2003, Burish et al 1992) declared that psychological reasons may also partly explain these results. Indeed, it was previously reported that relaxation and distraction techniques have significantly improved nausea and vomiting in breast cancer patients receiving chemotherapy (Molassiotis 2002). Acupressure is easily learnt and taught and patients should be informed about its potential role and taught how to apply it. Self-administered acupressure appears to have a protective effect for acute nausea (Ezzo 2007).

There have been recent advances in chemotherapy-induced nausea and vomiting using 5-HT_3 inhibitors and dexamethasone. However, many still experience these symptoms, and expert panels encourage additional methods to reduce these symptoms (Ezzo et al 2007). Research supports the effectiveness of acupuncture and acupressure for the treatment of chemotherapy-induced nausea and vomiting. Used in conjunction with current antiemetic drugs, acupuncture and acupressure have been shown to be safe and effective for relief of the nausea and vomiting resulting from chemotherapy (Collins and Thomas, 2004).

Studies have confirmed that the key to successful management of CINV is to prevent symptoms before they occur (Goodman 1997, Morrow et al 1998). Assessment evaluation of a cancer patient's general condition and a determination of how he or she feels is the first step in managing symptoms (Dodd et al 2001). Different approaches to symptom assessment may be adopted, from unstructured communication between patients and healthcare professionals to the use of documentation such as checklists or diaries. Research suggests that systematic assessment of symptoms is associated with reduced symptom distress over time (Sarna 1998).

Chemotherapy-induced nausea and vomiting is classified as either "acute" within 24 h post chemotherapy or "delayed" nausea that occurs on Days 2–5 of the chemotherapy cycle is particularly troublesome because there is no reliable pharmacological treatment for this problem (Morrow et al 1996, 1998). The American Society of Clinical Oncology (ASCO) recommendations include giving potential 5-HT_3 receptor antagonists plus corticosteroids before chemotherapy to patients receiving chemotherapy that are at high risk of emesis. Nevertheless, many patients still experience nausea and vomiting related to chemotherapy. Therefore, the expert panels emphasize the need for evaluation of additional ways to reduce these symptoms (Gralla et al 1981, Hesketh et al 1998). The need for additional relief has led to interest in non-pharmacological adjuncts to drugs like acupuncture or acupressure. Combining antiemetics with other non-pharmacological treatments may prove more effective in decreasing nausea than antiemetics alone (Molassiotis et al 2006).

Acupressure at the P6 point is a value-added technique in addition to pharmaceutical management for women undergoing treatment for breast cancer to reduce the amount and intensity of delayed CINV (Dibble et al 2007). Implication for practice even with the best anti emetic pharmacological agents, 60% of cancer patients continue to experience nausea and vomiting when under going chemotherapy treatment (Collins et al 2004). Interestingly, several studies reviewed by Morrow and Roscoe (1997) have found that women, compared to men, are more susceptible to nausea caused by classical conditioning, as evidenced by the fact that women are more likely to experience nausea in anticipation of chemotherapy.

2. Statement of the Problem

Complete control of chemotherapy-induced nausea and vomiting (NV) remains elusive despite decades of research on pharmacological antiemetics. Nausea in particular remains a significant problem with as many as 75% of patients reporting the symptom at some point following their treatment. Approximately one-third of patients have nausea of at least moderate intensity resulting in a significant reduction in quality of life (QOL). Delayed nausea that occurs on Days 2–5 of the chemotherapy cycle is particularly troublesome because there is no reliable pharmacological treatment for this problem. Not surprisingly, considerable effort and interest continue to be focused on developing better control of NV.

Difficulty in completely managing chemotherapy-related nausea and vomiting may stem from the multiple pathways involved in the development of nausea and vomiting including the chemoreceptor trigger zone in the brain, dopamine receptors, personality, vestibular dysfunction, age, anxiety and psychological mechanisms. Despite advances in anti emetic research over the past decade and the introduction of 5-hydroxytryptamine 3 (5-HT3) and Neurokinin1-receptor (NK1) antagonists, chemotherapy-related nausea and vomiting remain significant problems for the patients, decreasing their quality of life and negatively affecting their treatment experience, and impacting physical, cognitive, social, emotional and role functioning.

3. The Importance of the Study

Early studies reported that patients cited nausea and vomiting as the most distressing symptoms when receiving chemotherapy. Beyond their distressing effects, severe nausea and vomiting can lead to nutritional deficiencies, dehydration, electrolyte imbalance and fatigue. Despite continuing improvements in anti emetic therapies, nausea and vomiting following chemotherapy treatment for CA remains a significant clinical problem for many patients.

Acupressure is a non-invasive, simple method that can be used with good results, no side effect or discomfort, and less cost in relieving NV among breast cancer patients receiving chemotherapy drugs. The measurement of patient perspective has become an important component of treatment evaluation in many areas of medicine. There is evidence that the patients´ view differs from their clinician's judgment. Thus there is a need to expand the outcome measures used. Using a questionnaire, which was deemed adequate by the patients, gave a high response rate and showed a wide range of symptoms associated with chemotherapy management.

Despite continuing improvements in anti emetic therapies, nausea and vomiting following chemotherapy treatment for CA remains a significant clinical problem for many patients. Since pharmacological treatments have failed to completely manage nausea and vomiting, exploring the complementary role of other, non-pharmacological, approaches that can be used in addition to pharmacological approaches becomes paramount. Evidence is emerging that the stimulation of acupuncture points, particularly the Neiguan (P6) acupuncture point is helpful in controlling NV. While no theory that is generally accepted by the scientific community adequately explains how stimulation of the P6 acupuncture point reduces nausea, recent reviews have concluded that the practice does provide relief for a significant proportion of patients.

4. Hypothesis

Breast cancer patients undergoing their second cycle of chemotherapy using acupressure wristbands in addition to anti emetics over 5 days will have significantly lower nausea, retching and vomiting compared to breast cancer patients receiving anti emetics only.

5. Materials and Methods

The study was approved by the Ethics Committee at the Faculty of Higher Education at An-Najah National University and the Ministry of Health, Nablus Palestine. One hundred twenty six women, 18 years of age or older who are beginning their second cycle of chemotherapy for breast cancer treatment and nausea/vomiting with their previous cycle are randomized prior to chemotherapy to one of three groups after obtaining the verbal informed consent.

Group 1, Acupressure to P6 point **(active) (n=42).** The P6 (Neiguan), a point located on the pericardial meridian, which is found three fingers' breadth (approximately 5 cm) proximal to the proximal flexor palmar crease, about 1 cm deep between the tendons of flexor carpi radialis and palmaris longus is supposed to have an effect on post-operative nausea and vomiting (A barefoot doctor´s manual 1990). A Sea-Band (Sea- Band UK Ltd., Leicestershire, England) carries a plastic pearl which is fastened to apply pressure on P6. Both forearms are used. These points are marked with water-resistant ink so that the bands could be properly replaced if removed. The areas are draped with a dressing during the stay in the hospital. The nurses giving chemotherapy and the nurses on the ward, although aware that stimulation is being performed, are not aware of the location of P6.

Group 2, Acupressure to none acupoint (placebo (n=42). A point on the dorsal side of both forearms, four fingers' breadth proximal to the proximal flexor palmar crease was used for placebo stimulation. These points were marked in the same way as with the active acupressure. Sea-Band was used for stimulation, and the

same precautions were taken to keep the stimulation blinded (see above).

Group 3, Usual care only (control) (n=42). These patients were informed in the same way as the acupressure and placebo groups. Instructions for care and assessment are the same, as are the registrations of nausea and vomiting at home.

All subjects will complete a daily log for 5 days containing measures of nausea and vomiting and recording methods (including antiemetics) used to control these symptoms.

5.1 Design

This is a multicenter, prospective, consecutive, double blind and placebo-controlled clinical trial.

5.2 Inclusion criteria

(i) A breast cancer diagnosis, stage of cancer I–III, (ii) beginning their second cycle of chemotherapy for breast cancer treatment, (iii) had nausea/vomiting with their previous cycle, (iiii) willing to sign a consent form.

5.3 Exclusion criteria

(i) women received palliative chemotherapy, (ii) life expectancy is less than 3 months, (iii) had metastatic disease, (iiii) suffered from bowel obstruction, (v) undergoing concurrent radiotherapy or interferon treatment,

5.4 Randomization

After agreeing to participate in the study, the patients were randomised using the envelope method. Accordingly, a pack of sealed envelopes including a card with either the word 'acupressure group', "placebo group" or 'control group' written on it, was given to a staff nurse unrelated to the study; the patient will pick one envelope after she agrees to take part in the study. Depending on which card was selected patients allocated to their respective group.

5.5 Blindness

The Sea-Bands wrapped with a dressing bandage during the trial period. Neither the observer nor the subjects know if P6 or placebo stimulation was given.

5.6 Prophylactic antiemetic treatment

All patients received standard antiemetics before chemotherapy with a 5-HT_3 receptor antagonist (granisetron 3mg) and dexamethasone 4mg.

Group (1) received granisetron 3mg and dexamethasone 4mg, plus Acupressure to P6 point,

Group (2) received granisetron 3mg and dexamethasone 4mg, plus Acupressure to none acupoint (placebo).

Group 3 received granisetron 3mg and dexamethasone 4mg, and usual care only ***(***a control event group***).*** The drugs administered intravenously over 2—5 min immediately before induction of chemotherapy.

5.7 Setting

Patients are recruited from three oncology centres located throughout the West Bank (Al Watani Hospital in Nablus, Jeneen & Biet Jala Hospitals). These Clinical Oncology centres are potentially eligible for the study.

5.8 Intervention

Acupressure wristbands (Sea-Band™, Sea-Band Ltd., Leicestershire, UK) were used (Fig. V). These bands are elastic wrist bands with a 1 cm protruding round plastic button (stud). Patients wear the wristbands with the stud pressing the P6 acupoint, which is located on the anterior surface of the forearm, approximately three-finger width up from the crease of the wrist between the tendons of the palmaris longus and flexor carpi radialis. Wrist bands are used bilaterally.

5.9 Measures

At the time of consent, patients provided demographic information about the patients' age, marital status and education, details concerning prior experience with NV, for example, nausea during pregnancy, susceptibility to motion sickness, and so on, menstruation, and smoking. Clinical data included the chemotherapy regime and antiemetics used. The patients were asked to assess their degree of nausea during administration of chemotherapy in the hospital. Nausea and vomiting were measured by a patient report diary developed for this purpose by (Burish et al 1987, Carey and Burish 1988). Each day was divided into 4 segments (morning, afternoon, evening, and night) and patients reported the severity of nausea and number of vomiting episodes for each period on the day of treatment and on the four following days (20 total reporting times).

Severity of nausea was assessed on a 7-point rating scale, anchored at one end by 0 = "Not at all nauseated" and at the other end by 6 = "Extremely nauseated." The description "Moderately nauseated" was

centred on the scale above the 3. Patients were given the questionnaires to complete at home over the five days immediately following treatment and returned them to the practice site. Anti emetics rescue medication was used and the number of vomiting episodes were recorded for the same time intervals as part of the diary.

5.10 Quality of life instrument: FACT-G

QOL was assessed using the Functional Assessment of Cancer Therapy Scale-General (FACT-G). The FACT-G is a 27-item scale (higher scores = better QOL) developed specifically for use in cancer clinical trials (Cella 1993). The FACT-G consists of 5 subscales; physical well being (PWB; 7 items), social/family well being (SWB; 7 items), emotional well being (EWB; 6 items), functional well being (FWB; 7 items). It is used internationally and has undergone extensive psychometric testing: test/retest reliability coefficients range from 0.82 to 0.92, internal consistency of subscales measures range from 0.60 to 0.89) (Ward 1997). The FACT-G is designed for self-assessment to be rated on a 5-point Likert scale. Patients can complete the FACT-G within about 10 min. Each of the inventory questions is scored from 0 (worst possible QOL) to 4 (best possible QOL) with some items being reversed. In addition to an overall quality of life score (the sum of all items), there are subscales for the areas of physical well-being, social well-being, emotional well-being and functional well-being). Patients completed the measure four days after the day of chemotherapy and assessed QOL retrospectively since the treatment (Winstead-Fry and Schultz 1997). The sub-scores of the FACT-G were calculated according to the directions provided in the FACIT-Manual (all subscales are scored in such a way that higher values mean higher QOL (Cella 1993).

5.11 A feedback questionnaire

It was completed by patients at the conclusion of the study period concerning use of diary book, Quality of life instrument: FACT-G. Satisfaction and recommendations for the band(s). Participants were given questionnaires to complete at home, with instructions to return them back in the pre-addressed envelopes that were provided. Reminder phone calls were made to patients, if necessary. The study concluded with the return of data following the next chemotherapy treatment.

5.12 Assessment of patient satisfaction

Patients estimated their satisfaction with their NV treatment using a Lickert-type scale 0-6, in which 0 = very much dissatisfied, and 6 = very much satisfied. Overall patient satisfaction with the band and recommendation of using the sea bands as assessed by the feedback question asking whether the patients would recommend that other patients wear a band when receiving chemotherapy.

5.13 Procedures

The study was approved by the Ethics Committee at the Faculty of Higher Education at An-Najah National University and the Ministry of Health, Nablus, Palestine. Informed consent obtained from each subject. The study was double blind and the patients are randomised after accepting entry into the study. One group receives active treatment (n=42), one placebo treatment (n=42) and one group was used as a control (n=42).

A nurse who was not involved in caring for the patient postoperatively positioned the Seabands (SeaBand®, UK Ltd., Leicestershire, England) on both wrists at either the P6 point or on a non-acupoint just before the start of the chemotherapy. The wrists are wrapped for blinding. The patients were asked to wear the bands continuously for 24 hr. If the bands caused discomfort, they could be removed for 30 min every two hours. All patients received a 5-HT_3 antiemetic (granisetron 3mg) and Dexamethazone 4 mg on the day of treatment before administration of chemotherapy. Antiemetic medications taken during treatment days 2–5 were not regulated but were recorded in a patient diary.

Nausea and emesis were measured by a patient report diary, based on one developed by Burish (1987) that would be completed by patients over a five-day period. Each day is divided into four segments (morning, afternoon, evening, night) in each of which patients would report the severity of nausea and number of vomiting episodes for each period on the day of treatment and on the four following days. Severity of nausea was assessed on a 7-point rating scale, anchored at one end by 0 = "Not at all nauseated" and at the other end by 7 = "Extremely nauseated." (Morrow 1984, 1992). The patients were asked to assess their degree of nausea after administration of chemotherapy. Metoclopramide 10 mg is administered I.V. at the patient's request.

Research coordinator at the study site trained patients in the proper use and placement of the wristband. The P6 (Nei-Guan) was located on the pericardial meridian. P6 was located three fingers breadth (approximately 5 cm) proximal to the proximal flexor palmar crease, about 1 cm deep, between the tendons of flexor carpi radialis and palmaris longus. The Sea-Band® (Sea-Band UK Ltd., Leicestershire, England, UK) was used to stimulate P6. It carried a plastic pearl that applied pressure on P6. Both forearms were used. A point on the dorsal side of both forearms, four fingers breadth proximal to the proximal flexor palmar crease was used for placebo stimulation. These points were marked in the same way as for P6 acupressure. The Sea-Band® was used

for stimulation. The control group followed the same protocol as the P6 acupressure and the non-acupressure groups, but had no wristband and thus was not blinded. The Sea-Bands were covered with a dressing during the trial period. Neither the observer nor the subjects knew if P6 or placebo stimulation was given.

Participants were later given two questionnaires to complete at home, with instructions to return them back at the next chemotherapy treatment in the pre-addressed envelopes that were provided. Reminder phone calls were made to patients, if necessary. Following this, the patients in the P-6 acupressure group and placebo group carried a set of acupressure wristbands and were instructed to wear them bilaterally throughout the following 5 days taking them off only when they were having a shower or a bath. Separate analyses were planned to examine the efficacy of the wrist band(s) in controlling acute nausea (occurring on the day of treatment) and delayed nausea (occurring during Days 2–5) because these were clinically relevant distinctions in the treatment of chemotherapy-related nausea.

All patients completed the day-log every evening after the chemotherapy administration and for five consecutive evenings. Completed questionnaires were returned directly to the researchers when coming for their second cycle. Socio-demographic and clinical data were collected from the patients' medical notes.

5.14 Statistics and Data Analysis

Based on the effect size observed in past studies, 42 patients are required to achieve a power of 80% at an alpha value set at 0.05 (Cohen 1992).

Five outcomes related to wrist band efficacy are examined using t-tests or chi-square as appropriate. They are: 1) any vomiting, 2) peak severity of nausea on the day of treatment (acute nausea), 3) peak severity of nausea during treatment Days 2–4, (delayed nausea), 4) (QOL, and 5) amount of antiemetic medication taken at home. Data was coded and entered into SPSS for statistical analysis. Descriptive statistics calculated with all socio-demographic and clinical data.

The primary outcome variable for this study was the severity of nausea averaged across days 2–5 of treatment, that is, delayed nausea. Analysis of variance (ANOVA), with a significance level of 0.05, was used to compare the average nausea severity between the three treatment arms. We intended to compare the sham location group to the correct location group if the previous analysis is significant. Secondary study outcomes were the severity of nausea during the first 24 hours following chemotherapy (acute nausea) and the occurrence of vomiting during the same 24-hour period. Data for acute nausea was analyzed in the same way as delayed nausea. Exploratory analyses are planned with QOL and antiemetic medication used as the outcome variables.

5.15 Ethical Considerations

The study presented in this thesis is performed in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committee of the Faculty of Higher Education, An-Najah National University, and Ministry of Health Nablus, Palestine.

To randomise the treatment is an ethical dilemma as the patient was not allowed to decide over her treatment. Nevertheless, all patients were given both verbal and written information before considering participation in the study. It was made clear that participation was voluntary, could be terminated at any time and that confidentiality was guaranteed. For that reason, the ethical dilemma was deemed to be small. When predicting risk for vomiting for the patients in the control group there were some with more than 60% risk of NV, yet they do not receive any form of acupressure.

However, all patients were given allopathic prophylactic anti emetic and all the patients received anti emetics when required regardless of which group the patients were randomised to. That was why the ethical dilemma was deemed to be small.

The patients´ integrity may be threatened when performing continuous data collection. The results were presented in a way that ensured that it was not possible to identify any of the individuals. The study protocol concentrates on the patients' health and well-being. It is important to know the incidence, intensity so that the right symptom can be addressed.

Knowing which pharmacological and non-pharmacological preventive treatments for NV are beneficial and which are not will enable us to decrease the suffering for patients and the cost for society. The above made the ethical dilemma small in comparison with the expected benefits for the patients. To burden the patient with questions concerning nausea and vomiting takes time and strength. However, patients feel that they receive more attention and this could be regarded as positive. Furthermore, evaluation of nausea and vomiting as seen from the patients´ perspective, could lead to improvement in chemotherapy induced nausea and vomiting care for other patients in the future.

6. Results

One hundred and twenty sex patients were included in the primary data analysis.

6.1Demographic data (Table1) and risk factors for nausea and vomiting were shown in (table 2).

Table (1): Demographic characteristics of patients in treatment groups.

	Acupressure n=42	**Placebo n=42**	**Control n=42**
Age (ys) M(SD)	51(13)	53(12)	54(13)
Marital status			
Unmarried n (%)	4(10)	6(14)	5(12)
Married	29(69)	27(64)	27(64)
Widow	8(19)	7(17)	10(24)
Divorced	1(2)	2(5)	0
Children (n %)			
Yes	33(79)	30(71)	32(76)
No	9(21)	12(29)	10(24)
No. of children n (%)			
1-6	31(74)	31(74)	24(57)
7-12	11(26)	11(26)	18(43)
Accommodation (%)			
Alone	5(12)	4(10)	7(17)
With spouse	26(62)	22(52)	24(57)
With original family	8(19)	13(31)	8(19)
Others	3(7)	3(7)	3(7)
Education			
Primary	20(47)	18(43)	19(45)
Secondary	12(28)	8(19)	9(22)
Bachelor	4(9)	4 (10)	5(12)
Higher education	6(14)	10(24)	3(7)
Another	1(2)	2(4)	6(14)
Occupation			
Full time	2(5)	4(10)	3(7)
Partial time	3(7)	3(7)	2(5)
House wife	36(85)	34(81)	37(88)
Student	1(2)	1(2)	0(0)

The three groups were similar with respect to demographic characteristics, no statistically significant difference were seen between the groups, homogeneity of a group subjects has implicated for study design. (Table 1).

Table (2): Risk factors for nausea and vomiting in the acupressure, placebo and control groups.

Variable	**Acupressure (n=42)**	**Placebo (n=42)**	**Control (n=42)**
Health			
Chronic illness	33.3%	28.6%	28.6
No chronic illness	66%	71.4%	71.4%
Nausea in pregnancy	40.5%	33.3%	57.1%
Vomiting in pregnancy	40.5	33.3%	42.9%
Nausea in menstruation	21.4%	33.3%	9.5%
Menstruation vomiting	7.1%	2.4%	7.1%
Motion sickness	21.4%	28.6%	31.0%
Motion vomiting	21.4%	14.3%	21.4%
Smoking	2.4%	0	0

The above table clarifies percentage of risk factors for the participant among the three groups, no differences among the three groups in relation to the above risk factors.

6.2 Acute nausea and vomiting/retching:

Table (3): Incidence & severity of nausea, vomiting/retching of patients in the treatment groups during first 24 h following chemotherapy**.**

Day one, during the first 24 h following chemotherapy	**Acupressure (n=42)**	**Placebo (n=42)**	**Control (n=42)**	**P value 13acupressure compared to control**	**P-value acupressure compared to placebo**
Incidence of Vomiting & Retching n (%)	28 (67)	32 (76)	30 (71)	p= 0.6369	p= 0.3340
The mean number of acute emetic episodes	2.23 (1.25)	2.5 (1.81)	2.25 (1.94)	p= 0.9050	p= 0.1107
Incidence of acute nausea n (%) a dichotomous fashion (yes/no)	26 (62)	30 (71)	30 (71)	p= 0.3545	p= 0.3545
Accumulative incidence of nausea ≥3(0-6 scale) in the first 24hs of chemotherapy	18(43)	28(67)	24(57)	P= 0.01904	P= 0.0284
Nausea severity (0-6 scale) in first 24 hours after chemotherapy Mean (SD)	1.62 (2.04)	2.17 (2.09)	1.64 (1.99)	p= 0.8967	p= 0.0006

No significant differences were found in the incidence of acute nausea or emesis 24- h following chemotherapy by treatment groups. Significant difference was found in the severity of early nausea (0-6 scale) in the acupressure group M (SD) 1.62 (2.04) as compared to placebo group 2.17 (2.09), p=0.0006. (Table3). The incidence of moderate to extreme nausea ≥ 3 (0-6 scale) for the first 24hs of chemotherapy was significantly less in acupressure group18 (43) compared to both placebo 28 (67) P = 0.0284 and a control 24 (57) P = 0.01904. No significant differences in the incidence of acute vomiting & retching were found by treatment group 67% (28/42) in acupressure group and 76% (32/42) in the placebo group (p= 0.6369) (p=0.3340) compared to control group 71% (30/42) respectively. There is no significant difference of the mean number of acute emetic episode was seen between the groups. The mean (SD) number of acute emetic episodes in acupressure group 2.23 (1.25), p= 0.9050, placebo 2.50 (1.81) p=0.1107 compared to control 2.25 (1.94) respectively (Table 3),

5.3 Delayed vomiting: The results are accumulating covering the entire period.

Table (4): Incidence of delayed vomiting episodes: Days 2-5, n (%) in the three groups after chemotherapy

Incidence of vomiting days 2-5	**Acupressure (n=42) n(%)**	**Placebo (n=42) n(%)**	**Control (n=42) n(%)**	**p-value acupressure compared to control**	**p-value acupressure compared to placebo**	**p-value placebo compared to control**
Day 2	17 (40)	20 (48)	14 (33)	P=0.4976	P=0.5097	P=0.1823
Day 3	17 (40)	25 (60)	18 (43)	P=0.8248	P=.0809	P=0.1265
Day 4	9 (21)	14 (33)	12 (29)	P=0.4497	P=0.2212	P=0.6369
Day5	6 (14)	7 (17)	10 (24)	P=0.2664	P=0.7629	P=0.4152
The whole period	20 (48)	27 (64)	24 (57)	p= 0.3822	p= 0.1239	p= 0.5027

The whole period incidence of delayed vomiting episodes days 2-5 was 48% (20/42), 64% (27/42), and 57% (24/42) in the acupressure, placebo and control group respectively. No significant differences were found between the groups. (Table 4).

6.4 Delayed nausea: The results are accumulating covering the entire period

Table (5): Mean (SD) of delayed nausea severity (0-6) scale. Patients who scored their nausea >0. Comparison between the three groups for the days 2-5 after chemotherapy.

Mean (SD) Of delayed nausea severity (0-6 scale) patients > 0	**Acupressur (n=42)**	**Placebo (n=42)**	**Control (n=42)**	**P-value Acupressure vs control**	**P-value Acupressure vs placebo**	**P-value Placebo Vs control**
Day 2						
Morning	1.43 (2.01)	1.57(1.83)	2.33 (2.02)			
12:00	1.85 (2.05)	1.57 (1.87)	2.09 (1.97)			
18:00	1.80 (2.14)	1.40 (1.72)	2.30 (1.89)			
Before sleep	1.87 (2.06)	1.52 (1.82)	1.88 (1.90)			
Total Mean (SD)	**1.73 (1.56)***	**1.51 (1.87) †**	**2.75 (1.94)* †**	p= 0.0000	p= 0.1526	p= 0.0000
Day 3						
Morning	1.56 /1.98)	1.59 (1.87)	2.30 (2.10)			
12:00	1.87 (2.09)	1.40 (1.87)	2.38 (2.08)			
18:00	1.68 (2.04)	1.40 (1.83)	2.09 (2.05)			
Before sleep	1.87 (2.19)	1.21 (1.81)	2.02 (2.07)			
Total Mean (SD)	**1.74 (2.07) *** **	**1.39(1.84)***	**2.19(2.07) *†**	p= 0.0000	p= 0.0214	p= 0.0000
Day 4						
Morning	1.51 (1.81)	1.54 (1.84)	1.88 (1.96)			
12:00	1.39 (1.74)	1,23 (1.73)	2.04 (2.07)			
18:00	1.31 (1,66)	1.16 (1.72)	1.78 (1.84)			
Before sleep	1.31 (1.73)	1.07 (1.62)	1.52 (1.77)			
Total Mean (SD)	**1.37 (1.73)***	**1.25 (1.72) †**	**1.80(1.91)* †**	p= 0.0049	p= 0.4017	p= 0.0003
Day 5						
Morning	1.07 (1.61)	1.33 (1.83)	1.61 (1.80)			
12:00	0.97 (1.47)	1.19 (1.81)	1.40 (1.75)			
18:00	0.97 (1.58)	1.09 (1.69)	1.33 (1.81)			
Before sleep	0.97 (1.65)	1.14 (1.63)	1.23 (1.58)			
Total Mean (SD	**0.99 (1.57)***	**1.18 (1.74)**	**1.39 (1.73)***	p= 0.0000	p= 0.1541	p= 0.1395
The whole period (2-5 days) Total mean (SD	1.45 (1.73)*	1.33(1.66) †	2.03 (1.91)* †	p= 0.0002	p= 0.4116	p= 0.0010

*P < 0.05 when P6 acupressure is compared to control group.
**P< 0.05 when P6 acupressure is compared to placebo group.
† P< 0.05 when placebo is compared to control group.

Further analyses indicated that significant difference existed in the intensity of delayed nausea by acupressure group, mean (SD) 1.45 (1.73), p= 0.0002 as compared to control 2.03 (1.91) for the whole period. Significant difference also existed in the intensity of delayed nausea by placebo group mean (SD) 1.33 (1.66), p=0.0010 as compared to control 2.03 (1.91), here we noted a placebo effect (Table 5).

Table (6): Incidence of delayed nausea Days 2-5 in the three groups. Values given as n (%)

Incidence of delayed nausea day 2-5 Patients who answers yes	Acupressure (n=42) n(%)	Placebo (n=42) n(%)	Control (n=42) n(%)	P-value Acupressure vs control	P-value Placebo vs control
Day 2	25 (60)	24(57)	32 (76)	p= 0.1020	p= 0.0641
Day 3	24(57)	21(50) †	32(76) †	p= 0.0641	p= 0.0129
Day 4	22(52)*	22(52) †	31(74)* †	p= 0.0419	p= 0.0419
Day 5	17 (40)*	18(43)	26 (62)*	p= 0.0495	p= 0.0805
The whole period	17 (40)*	18 (43)	26(62)*	p= 0.0495	p= 0.0805

*P < 0.05 when P6 acupressure is compared to control group.
† P< 0.05 when placebo is compared to control group.

The acupressure group had a statistically significant reduction in the incidence of delayed nausea 40% (17/42) as compared to the control group 62% (26/42) (p= 0.0495) ((Table 6).

Table (7): Accumulative incidence of delayed nausea Days 2-5 ≥ 3 (0-6 scale) of moderate to very severe nature in the three groups. Values given as n(%)

Delayed nausea Day 2-5 ≥3 (0-6 scale)	Acupressure n=42 n(%)	Placebo n=42 n(%)	Control n=42 n(%)	P-value Acupressure vs control	P-value Placebo vs control
Day 2	18 (43)*	18 (43) †	28 (67)* †	p= 0.0284	p= 0.0284
Day 3	17 (40)	16)38)	22 (52)	p= 0.2740	p= 0.1884
Day 4	14 (33)*	13 (31)†	23 (55)* †	p= 0.0479	p= 0.0275
Day5	7 (17)*	12 (29)	18 (43)*	p= 0.0087	p= 0.1719
The whole period days 2-5	23 (55)*	22 (52) †	33 (79)*†	p= 0.0206	p= 0.0116

*P < 0.05 when P6 acupressure is compared to control group.
**P< 0.05 when P6 acupressure is compared to placebo group.
† P< 0.05 when placebo is compared to control group.

The percentage of the patients who had delayed moderate to very severe nausea day 2-5 (≥ 3 on 0-6 scale) in the acupressure group is 55% (23/42) (p= 0.0206), in the placebo group 52% (22/42) (p= 0.0116), a statistically significant reduction existed as compared to control 79% (33/42), here we noted as a placebo effect (Table 7)

*6.5 Delayed emetic episodes: The results are accumulating covering the entire period***:**
Table (8): Number of delayed emetic episodes Days 2-5 in the three groups. Values given as Mean (SD)

Mean (SD) of No. emetic episodes The patients who vomited only are included	**Acupressure (n=42) Mean (SD)**	**Placebo (n=42) Mean (SD)**	**Control (n=42) Mean (SD)**	p-value acupressure vs control	p-value acupressure vs placebo	p-value placebo vs control
Day 2						
Morning	1.5 (0.83)	1.78 (1.11)	2.45 (1.5)			
12:00	1.5 (0.83)	2.1 (1.44)	2.57 (1.38)			
18:00	2 (0.98)	2 (1.32)	2.27 (1.34)			
Before sleep	1.8 (0.91)	2 (1.16)	2.3 (1.10)	P=	P=	P=
Total	1.7 (0.88)	1.97(1.25)	2.39 (1.33)	0.0000	0.0907	0.0117
Day 3						
Morning	1.75 (0.92)	1.46 (0.839	2.38 (1.54)			
12:00	1.75 (0.99)	1.83 (1.05)	2.33 (1.37)			
18:00	2.22 (1.18)	1.46 (0.86)	3,00 (1.53)			
Before sleep	2.4 (1.30)	1.71 (0.81)	2.28 (1.15)	p=	p=	p=
The whole period	2.03 (1.09)	1.61 (0.88)	2.49 (1.39)	0.0035	0.0058	0.0000
Day 4						
Morning	1.12(0.51)	1.66 (0.76)	2 (1.21)			
12:00	1.40 (0.56)	1.33 (0.52)	2.33 (1.24)			
18:00	1.8 (0.73)	1.37 (0.61)	2.33 (1.19)			
Before sleep	1.66 (0.83)	1.6 (0.76)	2.66 (1.20)	p=	p=	p=
The whole period	1.49 (0.65)	1.49 (0.66)	2.33 (1.21)	0.0000	1.0000	0.0000
Day 5						
Morning	1.25 (0.43)	1.66 (0.85)	1.8 (1.08)			
12:00	1.66 (0.79)	1.66 (0.45)	2.33 (1.12			
18:00	1.5 (0.57)	1.00 (0.51)	2.04 (2.33)			
Before sleep	0.21 (0.57)	1.00 (0.51)	2.2 (1.01)	p=	p=	p=
The whole period	1.5 (0.64)	1.33 (0.58)	2.09 (1.13)	0.0001	0.2327	0.0000
The whole period 2-5 day	1.68 (0.86)*	1.6 (0.82)†	2.07(1.20)*†	p= 0.0109	p= 0.5900	p= 0.0020

*$P < 0.05$ when P6 acupressure is compared to control group.
† P< 0.05 when placebo is compared to control group.

The mean number of delayed emetic episodes days 2-5 was significantly less in the acupressure group mean (SD) 1.68 (0.86) as compared to control 2.07(1.20) p=0.0109 and less in the placebo group 1.6 (0.82) as compared to control P= 0.0020 (Table 8).

6.6 Requirement of rescue antiemetic:
Table (4.9): Requirement of rescue antiemetic in the three group's days 1-5

The whole period	**Acupressure (n=42)**	**Placebo (n=42)**	**Control (n=42)**	**P- value Acupressure vs control**	**p-value placebo vs control**
`Not required antiemetic	19	16	10	p=0.0389	p= 0.1568
Required antiemetic	23 (55)*	26 (62)	32 (76)*	p= 0.0389	p= 0.1568

*P < 0.05 when P6 acupressure is compared to control group.
Requirement of rescue antiemetic was significantly lower in P6-acupressure (55%, 23/42), as compared to control group (76%, 32/42) (p= 0.0389) (Table 9).

6.7 Analyses of QOL by using FACT-G. The results are accumulating covering the entire period:

Table (10): Comparison of the study outcomes by Analyses of QOL by using FACT-G

FACT-G (version 4)	**Acupressure (n=42)**	**Placebo (n=42)**	**Control (n=42)**	**P value Acupressure vs control**
Physical well-being (PWB)	16	15	15	
Social/family wellbeing SWB)	24	20	19	
Emotional well-being EWB)	16	15	17	
Functional well- being (FWB)	18	17	18	
Over all QOL score 108 point	74	67	69	p= 0.4720

Exploratory analyses of QOL by using FACT-G was shown that no statistically significant differences between groups were observed for the overall items response rate of the FACT-Scale which were 74/108, 67/108, 69/108 in the acupressure, placebo and control group respectively (Table 10). The FACT-Scale is considered to be an acceptable indicator of patient QOL as long as overall item response rate is greater than 80%.

6.8 Overall patient satisfaction and recommendations for other patients to wear acupressure bands

Table (11): Overall patients´ satisfaction with acupressure and if they would recommend other patients to wear bands when receiving chemotherapy.

	Acupressure (n=42)	**Placebo (n=42)**	**P-value 0.05**
Satisfaction with P-6 acupressure ≥ 3 (0-6 scale) n (%)	35 (81)*	27(64)*	p= 0.0471
Recommendation P-6 acupressure ≥ 3 (0-6 scale)	34 (79)*	26 (62)*	p= 0.0533

*$P < 0.05$ when P6 acupressure is compared to control group.

The patients were satisfied with the antiemetic treatment in (P6-acupressure, and placebo-acupressure). The percentage of the patients (≥ 3 on 0-6 scale) who were satisfied with treatment was 81% (35/42) in the P6-acupressure group, and 64% (27/42) in the placebo group (p= 0.0471). Percentage of the patients who would recommend acupressure treatment was 79% (34/42) in the P6-acupressure group, and 62% (26/42) in the placebo group (p= 0.0533). (Table 11).

7. Discussion

Findings from the present study confirmed that acupressure is efficacious for control of delayed chemotherapy related nausea and emesis and is a value-added method in addition to pharmaceutical management for women undergoing treatment for breast cancer. This is in accordance with the accumulating body of evidence related to acupressure during chemotherapy and shows that acupressure is a safe and complementary option in the management of chemotherapy-related nausea and vomiting (Roscoe *et al*., 2005; Shin *et al*., 2004; Dibble, 2000).

Our study is consistent with the study results of Dibble *et al* (2000) which were shown that finger acupressure may decrease nausea among women undergoing chemotherapy for breast cancer. Our study is also in agreement with the study of Roscoe *et al* (2006) who showed that acupressure wrist bands were efficacious and may be appropriate form of adjuvant therapy for nausea management for breast cancer patients, especially those who are most at risk for experiencing severe nausea following chemotherapy treatment

7.1 Acute nausea

Significant difference was found in the severity of early nausea (0-6 scale) at the first day in the acupressure group M (SD) 1.62 (2.04) as compared to placebo group 2.17 (2.09), p= 0.0006 which is consistent with the study of Nyström *et al* (2008) who demonstrated that acupuncture treatment in cancer patients can be associated with a significantly reduced intensity of nausea during a period of chemotherapy in their final phase of life.

The largest study of acupressure use for chemotherapy-related nausea and vomiting (n = 739) to date showed that the use of antiemetic pills was lower in the acupressure group (mean pills = 5.1) compared to the control group (mean pills = 9.7). This result is in agreement with the result of our present study regarding the requirement of rescue anti emetics which was significantly lower in P6-acupressure (55%, 23/42), compared to

control group (76%, 32/42) (p= 0.0389). However, there were some key differences between this study and our study in that some patients in the latter study received cisplatin based chemotherapy, which is considerably more emetogenic and difficult to manage than the types of chemotherapy used in the present study. Also, the Roscoe et al. Study (Roscoe, 2003) used patients with different cancer diagnoses, hence it was not as homogeneous as our study. It also seemed that their patients used mainly dexamethasone/other corticosteroids for the management of delayed nausea and vomiting whereas all of our patients received dexamethasone once. It is well known that dexamethasone is highly effective in managing delayed nausea and vomiting, although many clinicians, are sceptical of the use of steroids for prolonged periods of time. Hence, the use of dexamethasone may have contributed to the better control of nausea and vomiting in the study by (Roscoe *et al*., 2003), minimising the possible effect of wrist Bands. Such use of dexamethasone is a key factor to consider in future antiemetic trials of this kind.

In our study, no significant differences were found in the incidence of acute nausea or emesis 24- h following chemotherapy by treatment groups. This is inconsistent with the pooled results of 11 randomized controlled trials evaluating acupuncture-point stimulation plus antiemetic for chemotherapy-induced nausea and vomiting showed a significant reduction in the proportion of patients experiencing acute vomiting (Esso *et al*., 2005). On the other hand, in the current study acupressure seems to reduce chemotherapy-induced acute nausea severity A significant difference was found in the severity of early nausea (0-6 scale) in the acupressure group M (SD) 1.62 (2.04) as compared to placebo group 2.17 (2.09), p= 0.0006, this is consistent partially with the study of Ezzo *et al* (2005) who showed a marginal statistical significance for reducing severity of acute nausea.

Although other studies have also shown positive (and negative) effects with the use of acupressure in managing chemotherapy-induced nausea and vomiting, they are not easily comparable with the current study, as the method of acupressure differed. Past studies have used either finger acupressure and use of more than the P6 point (Dundee *et al*., 1991), or use of the Relief band / transcutenuous electrical nerve stimulation at the P6 point (Pearl, 1999, Treish *et al*., 2003; Roscoe *et al*., 2005). Mixed chemotherapy protocols and antiemetics used also make comparisons difficult. Furthermore, in another study by Roscoe *et al* (2005), where gender and type of chemotherapy were controlled, the placebo control group used an active Wrist Band, which may have led to the negative findings reported. It may be that constant pressure on the P6 point (as in the acupressure Wrist Bands) may produce better results than pressing the stud only or using electrical nerve stimulation to the point (as in the Relief Band).

7.2 Acute vomiting

In the current study, no significant differences were found in the incidence of acute emesis 24- h following chemotherapy by treatment groups. This finding is consistent with Dundee and Yang (1990) found that acupressure, by itself, was not sufficient to prevent vomiting in chemotherapy patients. Our results also are in agreement of Roscoe et al, (2005) who did not show that acupressure bands were efficacious when used as an adjunct to pharmacological anti emetics for the control of the incidence of chemotherapy-related vomiting in female breast cancer patients.

7.3 Delay nausea

Incidence of delayed nausea was significantly different among groups, with 55% of the acupressure group, 52% of the placebo group, and 79% of the control group $p<0.05$). Both the true acupressure and placebo acupressure groups were significantly different from the control group. Our results are consistent with study results of Ferrara-Love *et al*., (1996).

Patients randomized to the acupressure group had significantly less delayed nausea on (Days 2–5) of treatment than patients in the control. This reduction in nausea, however, did not extend to the acute phase following treatment (Day 1), nor was there a reduction in emesis. It cannot be ascertained from our data why the bands were helpful on (Days 2–5) of treatment but not on the first day. It may be related to the fact that the acute and delayed treatment-related nausea have different etiologist. So our results were not consistent with the study of (Roscoe *et al.*, 2003).

Our results are consistent with the results of Pearl and colleagues (1999) who examined the efficacy of acu-stimulation in 42 patients in a randomized, double-blind, placebo- controlled crossover trial, with a follow-up. For the 18 patients who completed the crossover component of the study, patients in the active band cycle, as compared to the placebo band cycle, reported a significantly lower severity of nausea during the second through fourth post-treatment days (O`Brien *et al*., 1996). Our results are consistent with the results of study there acupuncture combined with antiemetic which can effectively decrease the incidence and degree of cisplatin-induced delayed nausea and vomiting (Sima & Wang, 2009)

7.4 Delayed emesis

Our results regarding the mean number of delayed emetic episodes days 2-5 was significantly less in the

acupressure group M (SD) 1.68 (0.86) as compared to control 2.07(1.20,) p=0.0022 and less in the placebo group 1.6 (0.82 as compared to control, 2.07(1.20) P= 0.0005. This result is consistent with the study of Shen et al, (2000) which showed that the number of emesis episodes occurring during the 5 days was lower for patients receiving electro acupuncture compared with those receiving minimal needling or pharmacotherapy alone?

Patients in acupressure & placebo groups reported substantially lower rates of delayed nausea compared to patients in the control group, thereby indicating the presence of a powerful placebo effect. This is in consistent of a study (Alkaissi,1999) of PONV which had a similarly-designed 3-arm acupressure band study of 60 patients undergoing minor outpatient gynaecological surgery also it was reported positive results for placebo bands (Alkaissi,1999). Patients randomized to both the active acupressure band condition and to the placebo band condition had significantly less postoperative nausea than patients randomized to the no band control group (P= 0.05). There were no differences in the amount of nausea reported between the two acupressure band groups (Alkaissi, 1999).

In the current study no significant differences were found between the groups in the incidence of delayed vomiting episodes days 2-5, this was consistent with other studies in which no significant differences were found between the groups and delayed symptoms remain a problem for many cancer patients (Dibble 2003, 2004, Roscoe et al., 2005)

7.5 Quality of life

Nausea has obvious consequences on the quality of life, and it is not unusual for patients to experience nausea as a greater problem than pain (Strang *et al*., 1999). Therefore expert panels (Gralla *et al*., 1999; Hesketh et al., 1998) emphasize the need for additional ways to reduce symptoms. Chemotherapy induced nausea and vomiting can impair a patient's quality of life **(**Osoba, 1997**),** cause emotional distress, (Love *et al*., 1989**)** and aggravate cancer-related symptoms

In our study, no statistically significant differences between groups were observed for the overall items response rate of the FACT-Scale which were 74/108, 67/108, 69/108 in the acupressure, placebo and control group respectively which is inconsistent with the other study which showed that psychological well-being improved in women with breast cancer randomized to treatment with either applied relaxation and electro-acupuncture. On the other hand, our study is in complete agreement with the findings of Roscoe *et al* (2005).

8. Conclusion

We conclude that acupressure showed benefit for delayed nausea and the mean number of delayed emetic episodes, but not for the incidence of delayed vomiting, early vomiting or for acute nausea

Acupressure, therefore, may offer an inexpensive, convenient, self- administered intervention for patient on chemotherapy to reduce nausea and vomiting at home on days 2-5 of chemotherapy.

It is not clear why acupressure was effective for delayed nausea and not the incidence of delayed vomiting, but some trials for other kinds of nausea and vomiting have produced the sham outcome. It may be that, to influence vomiting, stronger form of P6 stimulation is needed. Acute nausea remains a problem even with the use of current antiemetic. It is not known why acute symptoms are so difficult to treat with conventional medications, but it is apparent that acupressure affects little for acute nausea induced by chemotherapy treatment of cancer patient.

9. Recommendation

P6- Acupressure is well-tolerated and effective as an adjunct in reducing chemotherapy-related nausea. Based on our results, we conclude that P6-acupressure, as an addition to standard, modern antiemetic therapy, has reduced delayed emesis in female patients undergoing doxorubicin- based chemotherapy. It is an alternative means of therapy aside from conventional or expensive antiemetic drugs and this is worthy of further investigation. The results of this study concur with that of other randomized controlled trials which showed that acupuncture-point stimulation reduced the proportion of patients experience in chemotherapy-induced vomiting.

Acupressure is easily learnt and taught and patients should be informed about its potential role and taught how to apply it. Leaflets about acupressure for the management of nausea and vomiting could be available in chemotherapy units so that patients who are interested to use such a technique are encouraged to come forward and learn more from nurses or other health professionals. This can add to the patients' options of their antiemetic approaches and empower them to be involved in the management of these distressing side effects..

10. Implications for Oncology Nurses

Studies about acupressure have concluded that acupressure is an important adjunct to pharmaceuticals in managing CINV (Dibble et al., 2000; Shin et al., 2004). Those studies as well as the current study suggest that oncology clinicians can include acupressure in their list of options for the management of CINV, especially delayed nausea and vomiting. Specific recommendations provided by oncology nurses are not only useful but

also are very appreciated by patients.

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