การป้องกันอาการคลื่นไส้อาเจียนในผู้ป่วยที่ได้รับการผ่าตัดทางนรีเวชวิทยาโดยการฉีดน้ำเกลือ 0.9% ที่จุดฝังเข็มเปรียบเทียบกับกลุ่มควบคุมด้วยวิธีสุ่ม

นางเล ลี

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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ACUPOINT INJECTION WITH 0.9% SALINE FOR THE PREVENTION OF NAUSEA AND VOMITING AFTER TOTAL ABDOMINAL HYSTERECTOMY: A RANDOMIZED, DOUBLE BLINDED, PLACEBO CONTROLLED TRIAL

Mrs. Li Lei

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Field of study : Health Development (Research)

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ลีเล : การป้องกันอาการคลื่นไส้อาเจียนในผู้ป่วยที่ได้รับการผ่าตัดมดลูกออกทางผนังหน้าท้องโดยการฉีดน้ำเกลือ 0.9% ที่จุดฝังเข็มเปรียบเทียบกับกลุ่มควบคุมด้วยวิธีการสุ่ม

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<u>วัตถุประสงค์</u> เพื่อศึกษาประสิทธิผลของการฉีดน้ำเกลือ 0.9 % ที่จุดฝังเข็ม 4 จุด เพื่อป้องกันการคลื่นไส้และอาเจียนหลังการผ่าตัดมดลูกทางหน้าท้อง

<u>รูปแบบการการวิจัย</u> การทดลองทางคลินิกแบบสุ่มทดลอง

<u>สถานที่ที่ทำการวิจัย</u> โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย

<u>ผู้ป่วยที่ร่วมในการวิจัย</u> หญิง 65 ราย ซึ่งมีระดับ ASA I – III และได้รับการผ่าตัดมดลูกออกทางหน้าท้องโดยการดมยาสลบ ผู้ป่วย 4 ราย ถูกตัดออกจากการศึกษา ผู้ป่วยที่เหลือ 61 รายได้รับการสุ่มเป็น 2 กลุ่มโดยผู้ป่วยและผู้ประเมินอาการ ไม่ทราบว่าผู้ป่วยอยู่ในกลุ่มศึกษาหรือกลุ่มควบคุม

<u>การรักษา</u> ผู้ป่วยที่เข้าข่ายการวิจัยได้รับการสุ่มเป็น 2 กลุ่ม โดยวิธีแบบบล็อคเมื่อสิ้นสุดการผ่าตัดมดลูกทางหน้าท้องและได้รับยาแก้คลายกล้ามเนื้อจากการดมยาสลบแล้วแต่ผู้ป่วยยังตื่นไม่เต็มที่ กลุ่มศึกษาได้รับการฉีดน้ำเกลือ 0.9% ที่จุดฝังเข็ม 4 จุดได้แก่จุด SP-6 และจุด ST-36 ทั้งสองข้าง ในขณะที่กลุ่มควบคุมไม่ได้รับการฉีดยาแต่จะมีพาสเตอร์ปิดที่จุดทั้ง 4 ทั้งสองกลุ่มเพื่อไม่ให้ผู้ป่วยหรือผู้ประเมินอาการทราบ

<u>ผลที่วัด</u> ประสิทธิผลของการฉีดน้ำเกลือ 0.9 % ที่จุดฝังเข็ม 4 จุดจะถูกประเมินใน 24 ชั่วโมงหลังการผ่าตัดโดยวัดอัตราการไม่เกิดอาการคลื่นไส้อาเจียนในสองกลุ่มเป็นผลปฐมภูมิ จำนวนการขย้อน จำนวนการอาเจียน และจำนวนยาแก้อาเจียนที่ใช้ใน 24 ชั่วโมงเป็นผลทุติยภูมิ

<u>ผลการรักษา</u> 1. ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติของอัตราการไม่เกิดอาการคลื่นไส้อาเจียนโดยรวม ในสองกลุ่ม 2. จำนวนการขย้อนและอาเจียนระหว่าง 6 – 24 ชั่วโมง หลังการผ่าตัดในกลุ่มศึกษาจะน้อยกว่ากลุ่มควบคุมอย่างมีนัยสำคัญทางสถิติ ($p < 0.001$ ในอาการขย้อนและ $p< 0.005$ ในอาการอาเจียน) 3. ผู้ป่วย 4 รายที่มีอาการขย้อนมากระหว่าง 24 ชั่วโมงอยู่ในกลุ่มควบคุมแต่ไม่มีผู้ป่วยขย้อนเลยในกลุ่มศึกษา 4. ไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติระหว่างสองกลุ่มในเรื่องเวลาที่มีอาการคลื่นไส้ ระดับคะแนนของอาการและจำนวนยาที่ใช้ 5. ไม่มีผลข้างเคียงจากการฉีดน้ำเกลือ 0.9% ที่จุดฝังเข็มทั้ง 4 จุด

<u>ผลสรุป</u> การฉีดน้ำเกลือที่จุดฝังเข็มไม่สามารถลดอัตราการเกิดอาการคลื่นไส้และอาเจียนโดยรวมภายใน 24 ชั่วโมงในผู้ป่วยที่ได้รับการผ่าตัดมดลูกทางหน้าท้องและได้รับการวางยาสลบทั่วไปได้ การพิสูจน์สมมุติฐานนี้จำเป็นต้องใช้ตัวอย่างการทดลองมากขึ้น เนื่องจากอัตราการเกิดอาการดังกล่าวในโรงพยาบาลจุฬาลงกรณ์มีไม่มากเท่าที่คาดตั้งแต่ต้น อย่างไรก็ตามการให้การป้องกันดังกล่าวสามารถลดความรุนแรงและจำนวนของอาการขย้อนและอาเจียนได้ในระหว่าง 6–24 ชั่วโมงหลังการผ่าตัด

ภาควิชา การพัฒนาสุขภาพ ลายมือชื่อนิสิต Lidei

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##4275390430: MAJOR HEALTH DEVELOPMENT
KEYWORD : ACUPOINT INJECTION / SALINE / NAUSEA / VOMITING / ABDOMINAL HYSTERECTOMY

LI LEI: ACUPOINT INJECTION WITH 0.9% SALINE FOR THE PREVENTION OF NAUSEA AND VOMITING AFTER TOTAL ABDOMINAL HYSTERECTOMY: A RANDOMIZED, DOUBLE BLINDED, PLACEBO CONTROLLED TRIAL
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THESIS CO-ADVISOR: SUPRANEE NIRUTHISARD M.D.
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Objective: To study the effectiveness of acupoint injection with 0.9% saline at the four acupoints for the prevention of nausea and vomiting after total abdominal hysterectomy under general anesthesia.

Design: A randomized, double-blinded, placebo controlled trial.

Setting: King Chulalongkorn Memorial Hospital, Thai Red Cross Society.

Participants: Sixty-five female ASA physical status I-III adult patients who underwent Total Abdominal Hysterectomy (TAH) under General Anesthesia (GA) were enrolled in the study, while 4 cases were excluded. Patients (n = 61) were double-blind randomized into two groups.

Intervention: The eligible patients were allocated into two groups by block randomization. At the end of hysterectomy and after the muscle relaxant was reversed but before the patient was fully alert, the patient in the study group received acupoint injection with 0.9% saline at four acupuncture points (both sides of PC-6 and ST-36) while the control group did not get acupoint injection.

Outcome measures: Efficacy was assessed by measuring complete response rate of PONV (no nausea, no retching, no vomiting, no rescue antiemetics) in both groups for the first 24 hours after the operation as main outcome. At the same time, the number of retching and vomiting as well as antiemetic rescue used within 24 hours in both groups were be recorded as secondary outcomes.

Results: 1. There was no statistical significant difference in the complete response rate(%) between the two groups (43.3% in acupoint group, 35.5% in control group with 95% CI of the difference: -16.7% to 32.3%). 2. The number of vomiting was significantly less in acupoint group compared to control group (P =0.024) in 24 hours after operation, especially during 6-24 hours (P = 0.005). 3. The patients who got retching were all in control group, with none in the acupoint group and the patients who got more 5 times vomiting in 24 hours were also in the control group. 4. There was no significant difference in times of nausea, nausea score and rescue using in both groups. 5. There was no incidence of adverse events in both groups.

Conclusion: Acupoint injection with normal saline does not reduce the overall incidence of nausea and vomiting in 24 hours after total abdominal hysterectomy under general anesthesia. However, it does reduce the frequency (number) of retching and vomiting during 24 hours after the operation.

Programme: Health Development
Field of study: Health Development (Research)
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Student's signature Li Lei
Advisor's signature Somjai Wangsuphachart
Co-advisor's signature

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CHAPTER 1

BACKGROUND AND RATIONALE

Postoperative nausea and vomiting (PONV) occur frequently and have become a critical issue in recent years. Patients find them quite disturbing, and PONV can cause complications like pneumonia, dehydration and retching that can break sutures, leading to infection. PONV is among the most common complications that occur during the immediate post-anesthesia phase[1,2], including post operation, especially involving gynecological surgery[3]. These distressing problems can affect both the real and the perceived course of a surgical procedure and often generate significant patient and family dissatisfaction with an otherwise flawless anesthetic.

Postoperative vomiting causes medical risks to a patient. Vomiting increases the risk of aspirating gastric contents with subsequent serious airway obstruction or aspirated pneumonitis. During emergence from general anesthesia, vomiting can precipitate serious laryngospasm with consequent hypoxemia. Forceful retching or vomiting increases intra-abdominal pressure, which in turn jeopardizes abdominal or pelvic suture lines. Vomiting also elicits a significant sympathetic nervous system response, which generates tachycardia and systemic hypertension. These hemodynamic changes increase risk of myocardial ischemia in patients with coronary artery disease.

Postoperative nausea is a particularly unpleasant sensation for the sufferer and is often the outstanding negative factor that a patient recalls about recovery from anesthesia. Unhappiness and discomfort caused by nausea intensifies other unpleasant elements of recovery, such as pain, boredom, frustration and fear.

PONV also has a negative impact on hospital staff or family after surgery. Dealing with vomiting patients might also marginally increase the risk to medical personnel from blood and secretion borne pathogens such as hepatitis and immunodeficiency viruses. PONV may delay discharge from the recovery room (RR) – thereby tying up human and material resources[4] -- and if it is severe enough, may require longer stay in the hospital. In addition, PONV can increase the cost of completing a surgical procedure, require additional antiemetic medications, extend the time a patient spends in the hospital, and thereby increase the overall expenditure. Although routine prophylaxis would seem appropriate, the choice of anti-emetic agents is wide, and some are too expensive to be cost-effective for routine use.

Antiemetic drugs have a variety of actions; including anticholinergic, antihistamine and antidopaminergic drugs. These actions can result in a wide variety of side-effects, which can occur even with low doses. These side effects include excessive sedation, hypotension, dry mouth, dystonic reactions, hallucinations, restlessness, dysphoria, tachycardia, and extrapyramidal symptoms.

Repeated efforts have been made to reduce the incidence and intensity of PONV for decades. Rowbotham, in his 1992 review of the management of PONV concluded, however, that the efficacy of currently available antiemetics remains poor.[5]

A growing concerning with the side effects and the high cost of the newer antiemetic drugs has led to renewed interest in nonpharmacological methods of treatment.

CHAPTER 2

Review of literature

2.1 Incidence of postoperative nausea and vomiting (PONV):[2]

Postoperative nausea and vomiting (PONV) complicates the lives of both patients and health care providers. The incidence of PONV varies between 20% and 88%[3,6,7,8] depending on a large number of poorly defined factors correlated with an increased incidence of postoperative emesis, including age, gender, body status, individual sensitivity, type of surgical procedure, technique and duration of anesthesia, and type of antiemetic regimen employed.

Reported studies of post anesthetic nausea and vomiting result vary so widely that discussion of an overall incidence for this problem loses real significance[9]. In addition, a wide variation is in large part caused by inconsistencies in the approach used to study this problem. A lack of universal agreement about what degree of symptomatology constitutes clinically significant nausea leads to a lack of comparability among studies. Incidence also varies across individual practitioners.

PONV has a remarkably high incidence, as high as 70-88% in women who undergo major gynecological surgery[10-20], and it can be especially troublesome in day surgery. At the very least the patient experiences discomfort, but symptoms may also persist causing a delay in returning to normal activities.

The variables are numerous, so it is difficult to construct reproducible, controlled studies with comparable patient groups and conditions. The study of balance, controlling bias, and understanding the risk factors are very important.

2.2 Risk factors for PONV: [20,21,22,23,24,25,26]

It is more effective to assess each patient in view of predisposing factors and then to qualitatively estimate the patient's individual risk of developing PONV.

Certain risk factors are unavoidable, such as those caused by the procedure and those associated with a particular patient. Since these cannot be modified, when they are present, diligent prophylaxis should be pursued. The choice of anesthetic is one factor over which the anesthesiologist has controlled.

2.2.1 Patient factors: [21]

Incidence of PONV seems to vary with several individual characteristics.

1. Age: Incidence seems lowest for infants, increasing through age – the peak is between 6-16 years old.[27]
2. Gender: Gender apparently influences the risk of postoperative nausea[21]. A perceived higher risk of nausea in women may be skewed by a relatively high incidence after gynecological procedures, which are only performed on women[20]
3. Menstruation: the cycle of menstruation may affect PONV, especially for the patients who are undergoing gynecological surgery.[28, 29]
4. History of motion sickness: people who often get motion sickness will have more chance to get PONV[30] ,

5. Previous PONV: Patients who had previous PONV will have more possibility to get PONV again [26]
6. Gastroparesis: e.g. diabetes, chronic cholecystitis, some neuromuscular disorders, bowel obstruction and a full stomach can cause PONV easily.[6]
7. Others : patients with anxiety, stress and a history of migraine will get PONV easily. Some studies showed obesity might relate to PONV as well. [21]

2.2.2 Anesthetic factors: [26]

Without question, exposure to anesthetic medications increases the risk of PONV.

It seems that the well-trained and experienced anesthesiologist correlates inversely with the incidence of PONV[31]. Regardless, the variation among practitioners confounds attempts to scientifically determine how various medications or anesthetics influence/affect the incidence of PONV.

- Certain Anesthetics have been associated with an increased risk of PONV:[3, 10, 17, 32,33,34,35,36,37]

1. Narcotics (pre-operative, intra-operative and post-operative[36]).
2. Potent inhalational agents, Etomidate, and Ketamine[6].
3. Mask anesthesia, with gastric distention can also increase the incidence of PONV.
4. Intubation and the Sellick's maneuver (cricoid pressure) can cause vomiting (via stimulation of the gag reflex). [38]
5. Nitrous Oxide (N_2O) increases the incidence of PONV. Proposed mechanisms include gastric distention (by diffusion into intestinal gas), vestibular stimulation (by diffusion into the middle ear), and catecholamine release (N_2O is a mild sympathomimetic).[8] [26, 39]

- Duration of anesthesia:

The length of surgery has also been correlated with PONV risk, due to the increasing duration of anesthesia.

Callesen et al[3] conducted a randomized controlled trial using combined epidural-spinal opioid-free anesthesia and analgesia for hysterectomies in 40 cases, concluded that opioid-free epidural-spinal anesthesia for hysterectomies caused less PONV, but analgesia intraoperatively was less effective compared to general anesthesia.

- General anesthesia:[37, 40]

1. Premedication:[41]

Using opioids such as morphine[42] or transmucosal fentanyl[43] for premedication increases the risk of PONV when compared to no premedication at all. Administration of Benzodiazepines, such as midazolam for preoperative sedation, does not increase the risk of nausea.[37]

2. Induction agents:

The choice of an induction agent for general anesthesia has a definite impact on the risk of PONV. Use of short acting thiopental seems less offensive than etomidate, which has been related to a high incidence of PONV[44].

3. Intubations:

Succinycholine was used for muscle relaxant in order to insert an endotracheal tube to control patient's ventilation.

4. Maintenance agents:

The role of nitrous oxide in postoperative nausea and vomiting in different patients is not the same[26,45, 46,47]. The general consensus is that nitrous oxide increases the

incidence of PONV in some patients, such as outpatient gynecological surgery[48], while some studies showed that it does not increase the incidence of PONV[8, 49].

The incidence of nausea does not seem to differ significantly whether isoflurane, enflurane, or desflurane is used for inhalation anesthesia[50]. When opioids such as fentanyl or morphine are added to an inhalation or the propofol-infusion anesthetic regimen is used, the incidence of PONV is not increased[51].

5. Reversal:

There is little evidence that neuromuscular relaxant has a significant impact on PONV. However, intravenous physostigmine for reversal of neuromuscular relaxants does increase the incidence of PONV, even when atropine is administered at the same time[52, 53]

6. Extubation:

Extubation also may increase PONV incidence, because of the irritation or traumatic process.

2.2.3 Surgical Factors: [21]

Certain surgical procedures carry a higher risk of PONV, such as increased risk of nausea after laparoscopy and other gynecologic procedures.

The following types of surgery have been found to correlate with a higher incidence of PONV: gynecological surgery, orchiopexy, and surgery for strabismus, middle ear, gastric and duodenal resection, cholecystectomy and extracorporeal shock wave lithotripsy.[20] [25]

2.2.4 Post-operative factors:

1. Post-operative narcotics (morphine);
2. Pain (especially pelvic);
3. Dizziness (dehydration, hypotension);
4. Motion (moving or sitting up too early);
5. Early oral intake;

So postoperative emetic symptoms are influenced by many factors, and these must be carefully controlled when studying PONV.

2.3 Treatment Options:

2.3.1 Most common anti-emetic drugs:[11]

1. Ondansetron (Zofran):
   - Cost: about 880 Bht / 4 mg dose
   - Mechanism: Serotonin (5HT3) receptor antagonist.
   - Similar agents: Granisetron, Tropisetron
   - Action: Found to be effective in both prophylaxis against and treatment of PONV. Some studies show the effects last up to 24 hours[54]. The optimal dose is 50 mcg/kg, or about 4 mg IV in the average adult [55]. All 5HT3 antagonists act in a similar manner, but their duration of action differs.
   - Side effects include headaches and constipation [56]. They usually do not cause sedation. One study[57] showed that addition of 8 mg of dexamethasone (decadron)

decreased PONV significantly, compared to ondansetron alone, but routine use of steroids needs careful consideration.

2. Metoclopramide:

- Cost 220 Bht. /10 mg dose
- Mechanism: central-dopamine antagonist for peripheral-increase gastric motility.
- Similar agent: domperidone (motilium)
- Some studies showed this agent to be effective in PONV prophylaxis -- others did not demonstrate a statistically significant difference from a placebo. The usual dose is 10 mg IV, but better results have been reported with doses of 15-20 mg IV. [58,59]

3. Droperidol (Inapsine)

- Cost: about 350 Bht. for 5 mg
- Mechanism: Dopamine (DA) antagonist.
- Similar agent: Prochloroperazine (compazine)
- Action: Droperidol is a highly effective antiemetic with a long duration of action (8 hours or more). It is a butyrophenone with some antagonist action at noradrenergic, serotonergic, and GABA receptors, and its primary antagonism is at dopaminergic receptors[60].
- Side effects include sedation (it is in the same medication class as haloperidol [Haldol]), agitation (especially in pediatric patients), dysphoria, and dyskinesias. Its use is contraindicated in patients with Parkinson's or other central dopamine depleting disease states. The usual dose is about 10-20 micrograms(mcg)/Kg (about 0.7-1.4 mg in a 70 KG adult). However, at this level, side effects are more prevalent, and sedation may delay emergence from anesthesia and/or RR discharge [60, 61]

2.3.2 Studies that compare agents:[62]

- Lin DM, et al. [58] studied Metoclopromide (Meto.) (0.15 or 0.25 mg/Kg) vs. Droperidol (Drop.) (0.075 mg/Kg) vs. placebo in 110 cases of pediatric strabismus surgery: N/V - Placebo 88%, Meto. 0.15 mg/Kg 68% (no significant difference), Meto. 0.25 mg/Kg 29% (significant difference), Drop. 33% (significant difference).
- Gan TJ, et al. [63] studied Ondansetron (Ondan.) (4 mg IV) vs. Droperidol (Drop.) (1.25 mg IV) vs. placebo in 120 adult orthopedic cases, double blinded: N/V - ondan. 17%, drop. 18%, both significantly lower than the placebo (45%), but there is no significant difference between the two treatment groups.
- Litman RS, et al. [64] studied Ondansetron (0.15 mg/kg) vs. Droperidol (0.075 mg/Kg) in 57 cases of pediatric strabismus surgery, double blinded: Emesis free - Ondan. 94%, Drop. 81% (no significant difference).

2.3.3 Studies that combine agents:

- Michaloudis D, et al.[65] studied combining agents with actions at different receptor sites, in sub-therapeutic doses (to minimize side effects). It was shown statistically to be as effective as a therapeutic dose of droperidol by Michaloudis, et al. in 71 GLP's - droperidol 0.5 mg + metoclopromide 5 mg + hyoscine 0.1 mg vs. droperidol 1.25 mg
- Mathia WJ, et al. [66] studied combining droperidol and metoclopromide, which did not decrease the incidence of N/V over droperidol alone.

Despite advances in anesthesia, prevention of postoperative nausea or vomiting (PONV) remains a continuing problem (high cost and substantial side effects). It is

important for surgical patients to improve their recovery, maintaining their confidence and satisfaction with the 'quality' of anesthetic care as well as reducing cost.

2.3.4 Alternative treatments:

Since most antiemetics have had undesirable side effects, or been expensive, alternative treatments for PONV have been investigated.

2.3.4.1 Ginger Root (Zingiber Officinale)

Herbal medicine has been practiced for thousands of years with mixed results. Modern pharmacology has isolated and quantified the active compounds permitting more precise dosing. Ginger root has been examined for efficacy in PONV prophylaxis in 2 placebo controlled, double-blinded studies:

1) Bone, et. Al.[67] studied 60 women for major gynecological surgery: The use of ginger root produced a statistically significant decrease in PONV compared to a placebo, with a response rate similar to metoclopromide. The dosage was 0.5 mg of powdered ginger root, in a capsule.

2) Phillips, et. Al. [68] studied 120 women after GLP: The use of ginger root produced a statistically significant decrease in PONV compared to a placebo, a response rate similar to metoclopromide.

While ginger root powdered capsules have not yet been available in most hospital settings, quality control of the product still needs to be considered.

2.3.4.2 Positive Suggestion[16, 69,70]

The human mind is a powerful tool, and positive suggestion is used by many people to help them change undesirable behaviors or reinforce desirable ones. Eastern "mystics" have demonstrated conscious control over autonomic functions, such as heart rate and metabolic rate. The power of positive suggestion to reduce PONV was examined in 2 controlled studies:

1). Williams et al [16] demonstrated significantly less N/V in patients who had received positive suggestions in a double-blind study of 60 women for major Gynecologic surgery,.

2). Lauder et al [70] demonstrated that the positive suggestion group required 16.5% less antiemetics than the control group in a prospective study of 266 patients,.

2.3.4.3 Acupuncture

1. What is Acupuncture?

According to a 1997 National Institutes of Health Consensus Conference on acupuncture, "Acupuncture describes a family of procedures involving stimulation of anatomical locations on the skin by a variety of techniques", such as needle, heat, cup, magnetic, laser and herb or other medicine [71].

2. Introduction of acupuncture therapy:

Acupuncture has been around for 3-5 thousand years. Traditional acupuncture theory is based on the flow of energy throughout the body. Traditionally it was believed that under normal conditions, this energy, known as Chi, flowed through the body through any of 12 channels known as meridians. The Chi was believed to heal and restore any

injury or illness that occurred in the tissues. If changes in the internal or external environment blocked the flow of Chi, energy would build up in certain body parts and would become depleted in the corresponding organs. This would lead to signs and symptoms of disease. The skilled acupuncturist would insert needles into the body at specific points along the channels (meridians) to restore the normal flow and distribution of the healing energy. Acupuncture was used to treat pain, but also was used to treat virtually any type of affliction known to man[72].

It seems hard to believe that inserting a needle in (for example) the leg just below the knee could help a patient suffering from a stomach problem. How could this be possible? Traditionally, the acupuncturist would theorize that some element such as wind, cold, dampness or fire had invaded the channels and interfered with Chi moving through the channels running to and from the stomach. This in turn would cause the stomach to function poorly and result in disease. The acupuncturist would insert needles and use other stimulation to restore and re-direct the flow of energy, this allowed the body to repair the damaged organ. Recently a panel of top scientists at the National Institute of Health (NIH in U.S), concluded that not only does acupuncture reduce pain, it also restores health to damaged and diseased tissues. Clinical studies suggesting its effectiveness for the treatment of various types of pain, depression, anxiety, spinally induced muscle spasm, stroke, gastrointestinal disorders, and drug addiction were also discussed[73]. More and more evidence is appearing in scientific literature supporting the use of acupuncture as an effective alternative to medical therapy.[73, 74]

How do needles inserted into the skin help to heal organs deep within the body? Modern acupuncture research has shown that acupuncture works by stimulating the

nerves running under the skin. The latest research shows that acupuncture can make changes in the chemistry of the body at the gene level.[72] Proper stimulation of the nerves can be used to either turn off the genes or stimulate their expression (activate the genes). So modern acupuncture can help body start to heal at the cellular level; even the genetic level.[75] While the scientific research on cellular or genetic change is needed.

Many studies concerning the effect of acupuncture on PONV have been undertaken.[76,77,78] These authors have overwhelmingly concluded that PC-6 acupuncture is effective as an antiemetic. Acupuncture has also been shown to be effective in the prevention of PONV in patients undergoing gynecological procedures.[79]

Several investigators have examined the efficacy in prevention of PONV in controlled studies: [80,81,82,83]

1) Fossoullaki, et. Al. [80] examined Transcutaneous Electrical Nerve Stimulation (TENS) at the P6 point (P6 TENS) in 103 females who had a hysterectomy suffered nausea and vomiting in 43% of the patients using a placebo and 23% ($p < 0.001$) of the patients using P6 TENS.

2) Dundee, et. al. [82] examined pressure at P6 vs. simple acupuncture at P6 vs. TENS at P6 vs. a placebo: All P6 methods showed statistically significant improvement in PONV compared to the placebo during the first 6 hours. Patients receiving TENS and acupuncture had significantly less N/V after 6 hours as well.

3) Ho, et. al.[83] examined the difference between TENS and electro-acupuncture at the P6 point vs. a placebo and prochlorperazine in 100 patients for GLP's: N/V in the placebo - 44%, P6 TENS - 36%, P6 electro-acupuncture-12%, prochlorperazine - 12%.

A systematic review by Lee and Done in 1999[84] suggested that non-pharmacological techniques are more effective than a placebo treatment in preventing

vomiting after surgery in adults, but not in children (See the table below). They concluded that non-pharmacological techniques are equivalent to commonly used antiemetic drugs in preventing vomiting after surgery in adults. The paucity of data regarding the use of non-pharmacological techniques led more researches to combine various types of stimulation at the PC-6 acupuncture point (i.e., manual acupuncture, electro acupuncture, transcutaneous electrical acupuncture and even acupressure stimulation) and analyzed the results collectively rather than for each individual type of acupoint stimulation. Another study, showed that acupuncture is not effective in children[85]. This may be questioned, as it is based largely on studies in which the therapy was administered while the child's central nervous system was profoundly depressed by general anesthetic drugs. The results may differ if children receive acu-stimulation while awake, or by applying a method that can prolong the acu-stimulation effect until children are conscious, or by adding more points which also have the antiemetic effect, such as ST-36, CV-12 and Liv-3[71]. The mechanism of stimulating acupoints for antiemetic action is unknown, but it may be related to the prevention of stomach and intestinal spasm and the release of emetic factors.

Table 2.1 :

Main results from meta-analysis of P6 acupuncture point stimulation compared with sham acupuncture for the prevention of postoperative nausea and vomiting

			Number of		Incidence with		
Patients	Patients without	Time	Patients	Studies	P6 stimulation (%)	Placebo (%)	95%CI
Adults	Nausea	Early	421	7	17	38	3.4 to 8.1
	Vomiting	Early	610	9	15	33	4.0 to 8.8
	Nausea	Late	187	3	13	40	2.5 to 6.5
	Vomiting	Late	290	4	18	27	no benefit
Children	Vomiting	Late	189	3	52	48	no benefit

Early time = 0-6 hours after operation, Late time = 6-48 hours after operation. Source: Lee and Done, 1999[84]

Stimulation of P6 point is claimed to reduce nausea and vomiting effectively, yet often in the western medical setting this treatment is limited due to a lack of acupuncture needles and by the inconvenience of stimulating points over an extended period (20-30 min.) manually or electrically. In addition many western medical practitioners are skeptical of acupuncture's effectiveness, an attitude which obstructs acupuncture practice in western hospitals. Consequently, there needs to be found an effective alternative method to stimulate the acupuncture points, a method which eliminates the need for acupuncture needles, at the same time, a method which is simple, convenient and acceptable to the western medical practitioner.

2.3.4.4 Acupoint injection:

Acupoint injection offers this alternative method: a therapy combining medicines with acupuncture. This method can be used to treat all diseases and medical problems which are suitable for acupuncture treatment by using the syringe to inject liquid medicine (such as herbs, drugs, vitamins, even a 0.9% saline and glucose mixture) into certain acupuncture points relevant to that particular disease or problem.[72] There are some studies which have shown that both acupuncture and acupoint-injection could improve patients' conditions, and also strengthen and prolong the therapeutic effect.[86] Cai Guowei and his colleagues performed a study in 1996 that compared the therapeutic effects of acupoint-injection (group 1 with herb-Ligustrazine, group 2 with saline) and electro-acupuncture (group 3) on blood rheology in coronary heart disease.[87] This study showed that injections of ligustrazine into Geshu (BL-17) had a most remarkable action in decreasing abnormally high data from indices of blood rheology in coronary heart disease. Guowei's group found the next best result came from the injection of saline, and the third best was using electro-acupucture stimulation of BL-17. In 1987, Wang, etc.

treated pregnant vomiting in 124 cases by injecting acupoints PC-6 and ST-36 with Vitamin B1; the first 64 cases (51.6%) were cured after one treatment, another 39 cases (31.5%) were cured after two treatments, and the last 21 cases (16.9%) were cured after 3 treatments. So all the patients' vomiting was controlled after three acupoint injection treatments at P-6 and ST-36 with vitamin B1[88]. However most of these studies were performed without a control group and included only clinical observation, so further clinical study under careful methodological control is necessary.

2.4 What will this research do?

The aim of this study is to test the effectiveness of the antiemetic action of acupoint injection with 0.9% saline applied at the acupoints (PC-6 and ST-36), an inexpensive and convenient method of administering acupuncture, in the first 24 hours following an abdominal hysterectomy under the general anesthetic process.

CHAPTER 3

RESEARCH QUESTIONS, OBJECTIVE AND CONCEPTUAL FRAMEWORK

3.1 Research Questions:

3.1.1 Primary:

Can the acupoint injection group get a 30%[7][89] better complete response (emesis-free, no PONV, no rescue antiemetic)[90] than the placebo group or not?

3.1.2 Secondary:

1). What is the difference of frequency of retching, and vomiting between the two groups? [91]

2). What is the difference of frequency and dosage of antiemetic drug use for severe PONV in both groups? [92]

3). Are there any adverse effects from acupoint injection? (Such as pain, hematoma, and neuritis).

3.2 Research Objective:

The aim of this study is to test the effectiveness of the antiemetic action of acupoint injection with 0.9% saline applied at the acupoints (PC-6 and ST-36), an

inexpensive and convenient method of administering acupuncture, in the first 24 hours following abdominal hysterectomy under the general anesthetic process.

3.2.1 To test the hypothesis whether acupoint injection with 0.9% saline at the acupoint (PC-6 and ST-36) could be more effective and safe to reduce the incidence of postoperative nausea and vomiting (PONV) in the first 24 hours following a total abdominal hysterectomy under general anesthesia.

3.2.2 To test whether acupoint injection with 0.9% saline at the acupoint (PC-6 and ST-36) could reduce the severity (vomiting > retching >nausea) and intensity (frequency) of PONV.

3.2.3 To prove that the requirement of antiemetic drugs is less in the acupoint injection group than the placebo group.

3.2.4 To discover any potential adverse effects of acupoint injection.

3.3 Research Hypothesis:

Acupoint injection with 0.9% normal saline is effective for the prevention of postoperative nausea and vomiting in the first 24 hours following a total abdominal hysterectomy under the general anesthetic process.

3.4 Conceptual Framework:

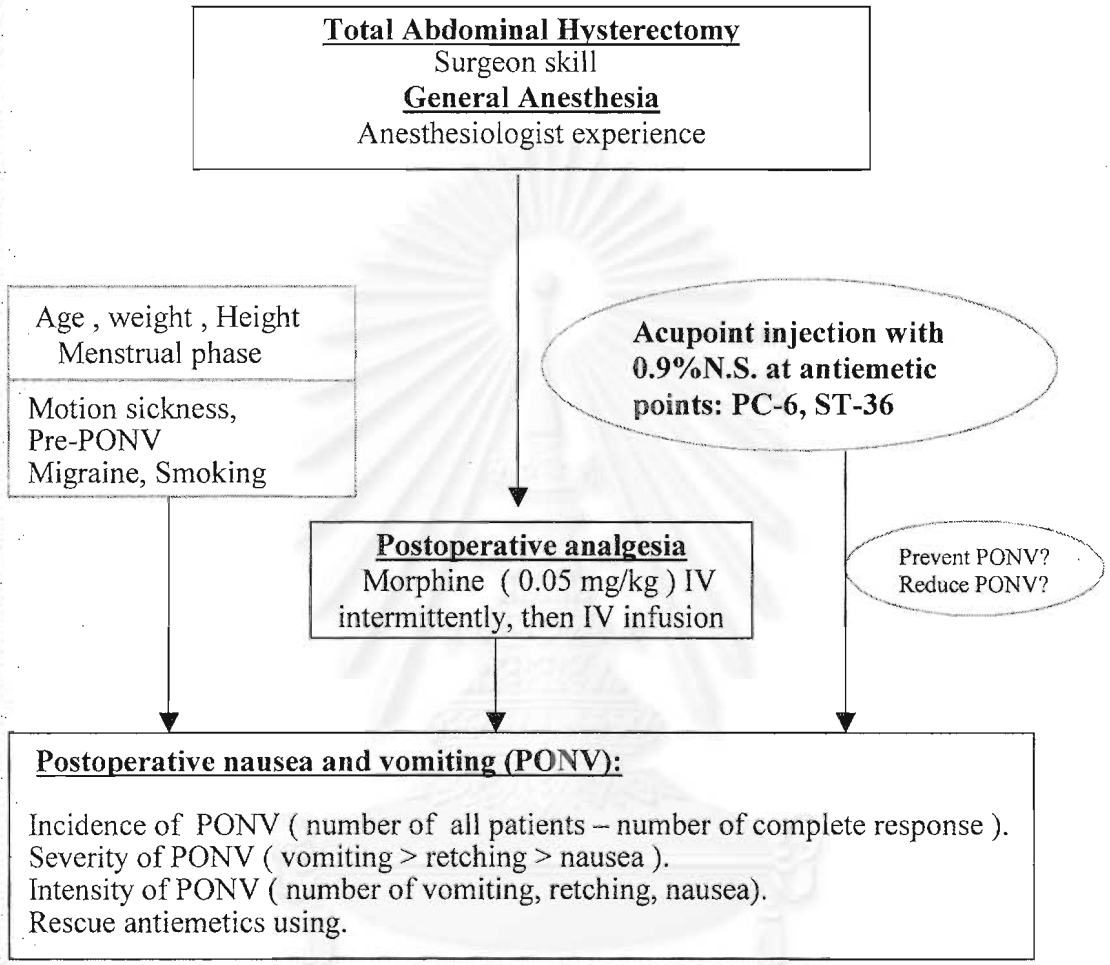


Fig. 3.4 Conceptual framework of the study

- Assumption :

Following the operational definition of this protocol, locating the acupoints correctly and well-trained nurses and family members to record the result truly are the keys for this research to prove the efficacy of antiemetic acupoint injection for prevention of nausea and vomiting.

3.5 Operational Definition:

3.5.1 Acupoint injection with 0.9% saline:

3.5.1.1 Material:

3ml disposable syringe, 0.4x12mm (27G× 1 / 2") disposable needle and 0.9% saline. According to the location of the acupoint[71] suggested to inject 1-5ml of saline into each point; here we choose 2ml for the PC-6 point and 3ml for the ST-36 point.

3.5.1.2 Location of the Acupoints: (see blow)

The two most common antiemetic points were selected[71][93] using the following formula:

a). Definitions: 1 "*cun*": The width of the individual thumb at the level of the interphalangeal joint. 2 "*cun*": Three fingers breadth, the second to fourth fingers, at the level of the third finger proximal phalangeal joint. 3 "*cun*": Four fingers breadth, the second to fifth fingers, at the level of the third finger proximal phalangeal joint.

b). PC-6 (Nei-Guan): The number 6 meridian point in the pericardium channel. It is located on the anterior surface of the forearm between the tendons of the extensor carpi radialis and palmaris longus, 2 *"cun"* (two widths of the interphalangeal joint of the patient's thumb) from the distal wrist crease.

PC-6 point functions: Relieves gastrointestinal spasm, controls gastric secretion, etc.[93]

c). ST-36 (Zhu San Li): When the knee is flexed, 3 *"cun"* distal from the mid point which is between the lateral tibial condyle and the patellar tip, one finger- breadth lateral from the anterior crest of the tibia.

ST-36 point functions: Balances the functions of stomach and intestine, release of pylorospasm[93].

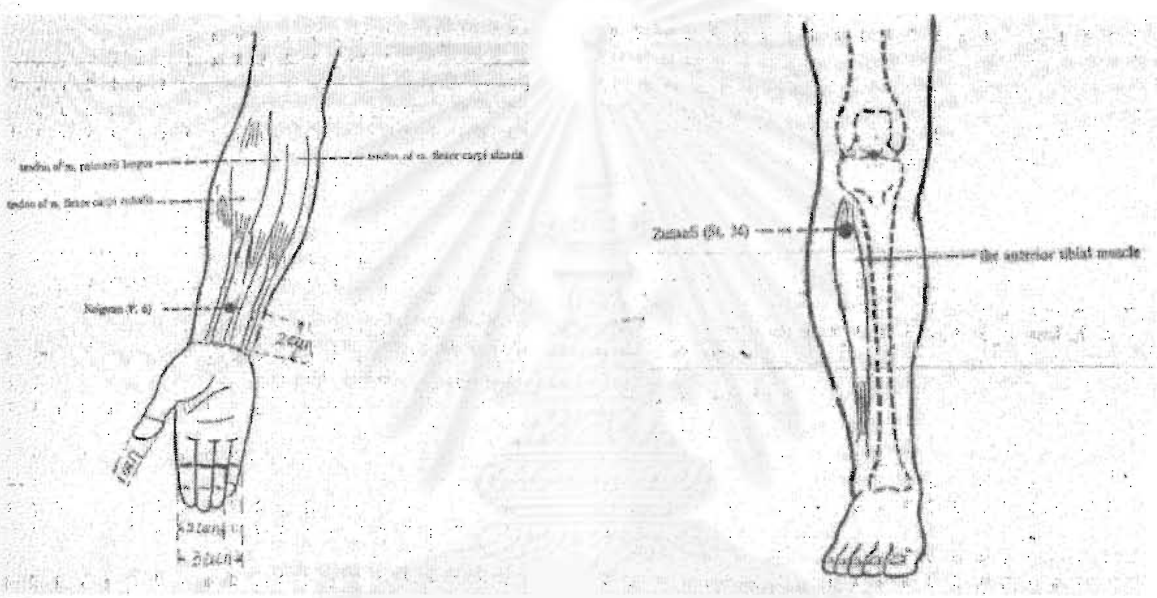


Fig. 3.5 Location of PC-6 and ST-36

3.5.1.3 Process :

1. General anesthetic process:

All patients underwent a standard general anesthestic process: Patients were premedicated with midazolam 0.05mg/kg, intravenously thirty minutes before starting anesthesia. *Thiopental* 5 mg/kg is used as the induction agent. The patients were intubated by using succinylcholine (1.5mg/kg). The maintenance was

achieved with 66% *nitrous oxide, isoflurane (1-2 %)*, vecuronium (0.1 mg/Kg), and *fentanyl* as requried by the patient.

2. Patients underwent a total abdominal hysterectomy.
3. All patients were reversed by *physostigmine (2.5 mg) and atropine (1.2 mg)*.
4. At the end of the operation, after the patients were extubated (muscle relaxant was reversed), the patients in the study group received acupoint injections with 0.9% saline, 2ml at PC-6 points and 3ml at the ST-36 points.
5. All the patients had identical adhesive tapes in place at the acupoints and were given a sentence to repeat twice as a test for the patient's memory before they were transferred to the recovery room.
6. For postoperative pain control, morphine (0.05 mg/kg, intravenously, every 10 minutes) was given as required until the patient's pain was well-controlled. After that morphine (20-30 ug/kg) was continuously infused for 24-36 hours. Oral paracetamol as needed was given to the patients capable of oral intake.
7. Post-operative period:

All episodes of PONV (nausea, retching, and vomiting) were recorded within the first 24 hours after operation, covering three time periods: 0-3 hours in the post anesthesia care unit, 3-6 hours and 6-24 hours in the general ward [89, 94].

8. Outcome assessment:

a). Primary outcome issue was complete response (emesis-free, no PONV, no rescue antiemetic medication).[89]

b). Nausea was defined as the subjectively unpleasant sensation associated with the urge to vomit. The severity of nausea will be graded from 0 (no nausea) to 10 (severe

nausea); that means the nausea score is evaluated by using a 10-cm visual analog scale (VAS).[95]

c). Retching was defined as the labored, spastic, rhythmic contraction of the respiratory muscles without the expulsion of the gastric contents.

d). Vomiting was defined as the forceful expulsion of gastric contents from the mouth.[6, 89, 94]

During the first 24 hours after surgery, if the nausea score was over 4, or the patient started retching or vomiting, or the patients requested, a rescue antiemetic-Metoclopramide (0.15mg / kg) would be given. If two doses of metoclopramide cannot improve the situation or the situation is out of control, the second rescue antiemetic-Ondansetron 0.08mg /kg would be given intravenously.

CHAPTER 4

RESEARCH METHODOLOGY

4.1 Research Design Diagram:

This is a randomized double-blinded controlled trial (blinded patients and assessors).

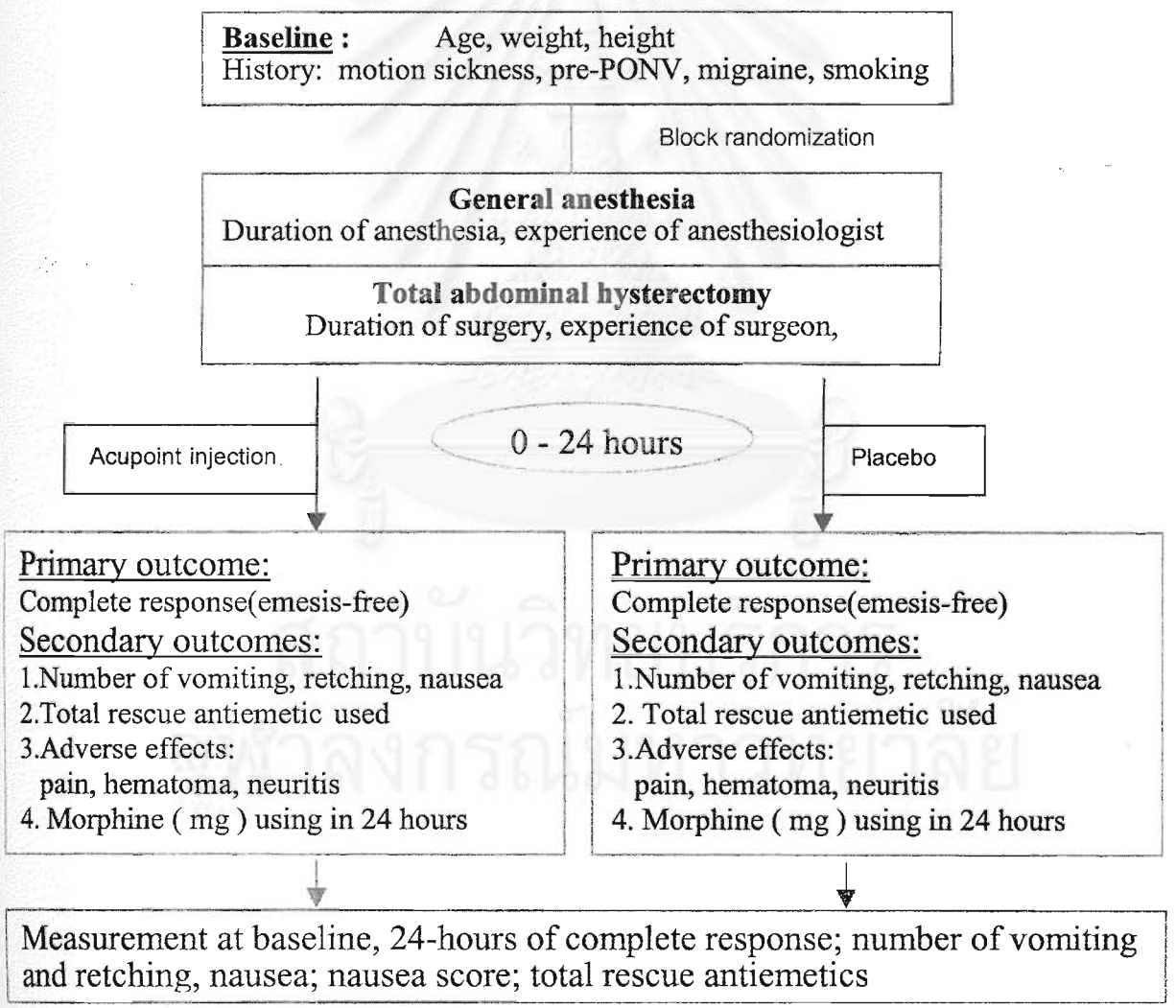


Fig. 4.1 Research Design Diagram

4.2 Population:

4.2.1 Target population: Females underwent total abdominal hysterectomy with general anesthesia.

4.2.2 Study population: Females who underwent total abdominal hysterectomy with general anesthesia at King Chulalongkorn Memorial Hospital in 2001 – 2002 who meet the following criteria.

4.2.3 Eligibility Criteria

4.2.3.1 Inclusion criteria: Female inpatients who

1. Were ASA physical status I-III
2. Were aged 20-60 years old.
3. Had body weight of 45-80 kg, height of 140-180 cm.
4. Agreed to participate, and understood the research purpose and procedure.
5. Consented to and accepted the acupoint injection method.
6. Had no history of allergy to drugs used in this study.

4.2.3.2 Exclusion criteria:

1. Patients who had gastro-intestinal disease, carcinoma.
2. Patients who had received any antiemetic medication within 24 hours before the surgery.
3. Patients who had experienced acupuncture within two weeks before the surgery.

4.2.4 Sample size:[89, 96]

Randomized controlled trial of the treatment to reduce the incidence of postoperative nausea or vomiting.

1. Data sets: Observations in one experimental group and one control group of the sample size.

2. Variable: suppose the incidence of PONV is 80%,[6,18,19] then complete response rate will be 20%.

So the success p_1 = 50%=0.5 means a complete response increase from 30% from 20%, up to 50% in the treatment group, while the failure p_2= 20%=0.2 is a complete response in the placebo group.

3. The average of p_1 and p_2 expressed as P=0.35=(0.5+0.2)/2 , 1-P=0.65

4. Z_α = 1.64 : α error = 0.05 (5%), therefore, 95% confidence desired (one tailed test) .

5. Z_β = 0.84, β error = 20%, therefore, 80% power is desired.

Difference to be detected (d): Based on the previous study by Yoshitaka Fujii,[89] it was calculated on the basis of 30% (0.3) difference in values for a complete response (no PONV, no rescue) will be regarded as the primary outcome between the acupoint injection group and the control group.

$$n/group = \frac{\left[Z_\alpha \sqrt{2P(1-P)} + Z_\beta \sqrt{p_1(1-p_1) + p_2(1-p_2)} \right]^2}{(p_1 - p_2)^2}$$

$$= \frac{\left[1.64 \sqrt{2 \times 0.35 \times 0.65} + 0.84 \sqrt{0.5(1-0.5) + 0.2(1-0.2)} \right]^2}{(0.5 - 0.2)^2} = 30$$

4.3 Experimental Maneuver:

4.3.1 Randomization method: Block randomization

The block randomization was designed to allocate the 60 patients to different treatments to achieve approximate balance of important factors, without sacrificing the advantages of random allocation. The details were:

1. After completing the block randomization list (randomized block size 4), using a table of random numbers, the code was set to allocate the patients into two groups. Group 1 was acupoint injection with 0.9% saline and group 2 was the control group.
2. When eligible patients registered to the trial, the investigator picked up the code as prepared.

4.3.2 Blinding Method

To avoid any biases in the comparison of the groups, the blinding method is desirable. In this study we used the double blinded design. Both the patients and the assessors did not know in which group of treatment the patients were enrolled.

4.3.3 Intervention

This study was conducted in King Chulalongkorn Memorial Hospital in Bangkok. The Institutional Review Board and Ethical Committee of the Faculty of Medicine,

Chulalongkorn University had approved the proposal protocol. The maneuvers in this study were:

1. The investigator assessed the patients who fulfilled the eligible criteria.
2. Patients or authorized family signed their informed consent after proper counselling and describing the details of the study including possible side effects of the acupoint injection by one of the investigators.
3. Randomization into parallel study-groups coded patients.
4. Both groups of patients were under the standard general anesthetic process.
5. Both groups of patients were under the standard total abdominal hysterectomy process.
6. At the end of the operation, muscle relaxant was reversed and the patient was extubated.
7. Group 1: Acupoint injection with 0.9% saline was performed by injection of 2 ml saline into PC-6 and then 3 ml saline into ST-36. Then identical adhesive tapes were applied to the acupoints.
8. Group 2: For the Placebo group, after the muscle relaxant was administered and the patient was extubated, the identical adhesive tapes were put on the same acupoints as group 1.
9. All the patients were given a sentence twice as a test for the patient's memory to made sure they did not remember whether they got acupoint injection or not before they were transferred to the recovery room.
10. For postoperative pain control, morphine (0.05 mg/kg, intravenously, every 10 minutes) was given as patient required until the patient' s pain was well-

controlled. After that, morphine (20-30 ug/kg) was continuously infused for 24 hours.

Post-operative period:

All episodes of PONV (nausea, retching, and vomiting) were recorded during the first 24 hours after the operation, covering three time periods: 0-3 hours in the recovery room, 3-6 hours and 6-24 hours in the general ward[89, 94].

4.4 Measurement:

Variables : Independent Variable = Group (acupoint group or control group)

Dependent Variable:

Complete response rate

Frequency of vomiting, retching, nausea

Nausea Score

Frequency of rescue antiemetics

4.4.1 Instrument and evaluators:

During the study period, there were four-scheduled follow up at baseline, 0-3 hours, 3-6 hours and 6-24 hours. The investigator recorded whether or not the patient acquired a complete response: if not, all episodes of PONV (nausea, retching, and vomiting), as well as the nausea score (NS) will be recorded within the first 24 hours after the operation, covering three time periods: 0-3 hours in the recovery room, 3-6 hours and 6-24 hours in the general ward [89, 94]

A descriptive Nausea Score (NS) was used to assess the severity of subjective nausea by a visual analog scale. The questions in the visual analog scale asked patients to mark the severity of their nausea: answers were based on a 10-point scale. The subjective nausea was classified from no nausea (0) to very serious nausea (10).

4.4.2 Outcomes Assessment

- Primary outcome:

percentage of complete response (no nausea, no retching and no vomiting at all)in both groups within 24 hours after surgery.

- Secondary outcome:

1. Numbers of nausea in both groups within 24 hours after surgery.
2. Numbers of retching in both groups within 24 hours after surgery.
3. Numbers of vomiting in both groups within 24 hours after surgery.
4. Rescue antiemetic medications given in both groups.
5. The severity of nausea was graded ranging from 0 (no nausea) to 10 (severe nausea).
6. Any adverse effects or complaints were recorded by the investigator who interviewed the patients.

4.5 Data Collection:

Each of these assessments was performed among the patients in both groups. Patients and nurses were informed that an antiemetic drug should be given when patients asked for it in the presence of intolerable nausea or retching or vomiting.

- Blinded patients and assessors:

Both patients and assessors (investigator and nurses) were unaware of the patient group allocation. The trained nurses performed the questioning and recorded it, and they were blinded to the study groups.

The incidence of nausea and vomiting during the 0-3, 3-6, and 6-24 hours were determined. The results were scored in a manner similar to that of Allen, Kitching and Nagle[97] as none, nausea, retching and vomiting. The severity of PONV was classified as vomiting > retching > nausea. If a patient experienced nausea , retching and vomiting, they would be recorded as having vomiting, If a patient experienced both nausea and retching they would be recorded as having retching. So the exact number of retching and vomiting were recorded. The severity of nausea was classified as none (0), mild (1-4) moderate (5-7) or severe (8-10), according to the Visual Analogue Scale[91]. The percentage of complete response was the primary outcome in each group at the end of the 24-hour period. At the same time, patient charts would be assessed for antiemetic requirements [97].

4.6 Data analysis :

4.6.1 Summarization of data

1. For continuous data , such as age, weight, height, last menstrual cycle(days), duration of surgery(min), duration of anesthesia(min), postoperative morphine(mg), nausea, retching, vomiting, rescue antiemetic, and severity of nausea (NS): The mean, SD and range were analyzed.
2. For categorical data, such as, history of PONV, motion sickness, migraine, smoking, complete response, and adverse effects: The number and / or percentage were presented and analyzed as appropriate. (Table 4.6)

4.6.2 Data presentation:

Table 4.6 Statistical analysis for demographic data and outcome variables

Variables	Types of Data	Data Summary	Statistical Test
Patient demographics in both groups:			
Age(year)	Continuous data	Mean , SD	
Height(cm)	Continuous data	Mean , SD	
Weight(kg)	Continuous data	Mean , SD	
Last menstrual cycle(days)	Continuous data	Mean , SD	
History: motion sickness,	Categorical data :	Number (%)	Chi-square or
PONV, migraine, smoking	Categorical data :	Number (%)	Fisher-Exact test
Duration of surgery(min)	Continuous data	Mean , SD	Student's t - test
Duration of anesthesia(min)	Continuous data	Mean , SD	(unpaired) or Mann-Whitney U test
Analgesic used postoperatively:			
Morphine(mg)	Continuous data	Mean , SD	Student's t - test (unpaired) or Mann-Whitney U test
Result Variables			
Primary outcomes:			
Complete response	Binary data	Number(%), 95% CI	Chi-square or Fisher-Exact test
Secondary outcomes:			
Nausea	Continuous data:	Mean, SD	Student's t - test
Retching	Continuous data:	Mean, SD	(unpaired) or
Vomiting	Continuous data:	Mean, SD	Mann-Whitney U
Rescue antiemetic	Continuous data:	Mean, SD	test
Severity of nausea	Continuous data	Mean, SD	
Adverse effects	Categorical data :	Number (%),	Chi-square or Fisher-Exact test

Statistical tests were performed as specified in the table. If the data could not hold the assumption (normal distribution) for t-test, the nonparametric test (Mann-Whitney U test) was used. For the 2x2 table, if any cell the expected value was less than 5, the Fisher-Exact test was used.

All the statistical tests were subjected to a significant level at 0.05 using SPSS/PC+ software version 10.0.

4.7 Ethical considerations:

4.7.1 Up to now the FDA has approved acupuncture single-use needles and some Chinese herbs in 120 countries in the world, such as the U.S.A. Canada, England, Australia, Japan, etc. In addition, the licenses for well-trained acupuncture practitioners are available in these countries.

4.7.2 The group of patients selected for this study is recognized as suffering a particularly high incidence of postoperative nausea or vomiting. Drug therapy is often complicated with central nervous system symptoms, and these can cause an extended stay in the hospital and also increase the cost of medical treatment. In contrast, acupoint injection with 0.9% saline has no side effects or drug interactions.

4.7.3 To locate the acupuncture points is the key step in acupuncture therapy. To set the acupuncture points in this study followed the standard of WHO approval.

4.8 Limitation:

The important factors, which may affect the result of acupoint injection treatment:

4.8.1 Acupuncture points selection: a well-trained practitioner is needed.

4.8.2 Time selection: The patients were preferred to be awake from the anesthetics, so the body systems could properly respond the stimulating of the acupoints. However, patients were still not fully alert after general anesthesia while the acupoint injection was performed, so the response might be limited.

4.9 Possible Obstacles:

A patient may feel uneasy about the possible pain from acupoint injection, therefore the time for injection was selected immediately after surgery and finished with general anesthesia, before the patient was fully awake and sent out of the operating theater, which may effect the result, because the nervous system was still not fully responding to acupoint injection.

To avoid medication interaction, we chose 0.9% saline to perform the acupoint stimulation, which may not be strong enough for the patient who was not fully wake from anesthesia. This also could affect the results.

4.10 Generalizability :

This study is trying to modified acupuncture treatment to be easy, convenient to perform, at the same time to prove its effectiveness. Any hospital or clinic which has acquired the acupoint injection technique can treat the patients. 0.9% saline is available in all hospitals or clinics around the world. Medical personnel can be trained to locate the correct acupoints easily. If the effectiveness of this study is proven, the acupoint injection technique can be trained in hospitals or clinics and can be applied in any situation to deal with nausea and vomiting, such as cancer patients who are undergoing chemo or radiation therapy.

4.11 Administration & Time schedule :

	April.2001 - April 2002	May – Aug.	Sep.2002
Sample study and data collection	→		
Data analysis and thesis writing		→	
Defense thesis			→

CHAPTER 5

RESULTS

5.1 Demographic characteristics of patients

This study was conducted at King Chulalongkorn Memorial Hospital in Bangkok, Thailand from April 2001 to March 2002. A total of sixty-five eligible patients underwent a total abdominal hysterectomy with general anesthesia, and were enrolled in this study. Four of them were excluded due to overweight (89 kg); under weight (41.3 kg); no reversal after operation and operation accident with an injured urine bladder. Actual patient number was 61 in this study, 31 patients were randomized into the control group and 30 patients into the acupoint group.

1. The demographic data of two groups are listed in Table 5.1. Acupoint group and control group were similar in age, height, weight and last menstrual cycle, so both group were comparable.

Table 5.1 Distribution of demographic data between two groups

Variables Patients		Acupoint Group N = 30	Control Group N =31
Age (years)			
	Mean (SD)	44.0 (5.95)	44.4 (5.13)
	Range	29-54	31-57
Height (cm)			
	Mean (SD)	154.9 (5.95)	153.5 (4.93)
	Range	145-168	145-165
Weight (Kg)			
	Mean (SD)	58.7 (8.54)	59.5 (8.92)
	Range	45-75	45-75
Last menstrual cycle (days)			
	Mean (SD)	17.6 (8.29)	21.1 (13.72)
	Range	9-26	7-35

2. Several factors that could affect the result of the study, hence the analysis of these factors (migraine, motion sickness, smoking, and history of postoperative nausea and vomiting) were under consideration.

According to Table 5.2 the Chi-square test was used to assess the difference between the two treatment groups. The result showed that there was no statistically significant difference in migraine, motion sickness, smoking, or history of postoperative nausea and vomiting between the two groups.

There was only one case of migraine in the control group and no case in the acupoint injection group. The number of motion sickness cases in both groups was not significantly different. For smoking, there were two cases in the acupoint- injection group and no case in the control group. The history of postoperative nausea and vomiting in the two groups also was considered, the analysis showed that there was no significant difference between two groups ($p > 0.05$)

Table 5.2 Proportion for the factors, which could affect the outcome of study in both groups

	Acupoint Group (n=30)	Control group (n=31)	P- value
Migraine (%)	0%	3.2%	> 0.05
Yes	0	1	
No	30	30	
Motion Sickness (%)	0%	0%	NA
Yes	0	0	
No	30	31	
Smoking (%)	6.7%	0%	0.238
Yes	2	0	
No	28	31	
History of PONV (%)	6.7%	12.9%	0.671
Yes	2	4	
No	28	27	

* Using 2x2 tables, since every item had 2 cells' expected count less than 5. Fisher's Exact Test was used to test the each item's difference.

3. The distribution of duration of surgery and anesthesia between two groups showed that there was no statistically significant difference with the mean 89.8 ± 26.96 and 113.1 ± 27.44 ($p > 0.05$). The postoperative morphine usage was recorded for 24 hours. According to the distribution shown in table 5.3, there were no significance differences between the acupoint group and the control group.

Table 5.3 Distribution of duration of surgery, anesthesia and morphine between two groups

	Acupoint Group n=30	Control Group n=31	Total n=61	P-Value
Duration of surgery (min):	*89.8 (26.96)	92.6 (33.11)	91.2 (30.02)	.868
Duration of anesthesia (min)	113.1 (27.44)	117.3 (24.81)	115.2 (31.21)	.767
Morphine (mg)	35.8 (6.18)	35.9 (4.85)	35.8 (5.5)	.988

* Mean(SD), Using Mann-Whitney U test

5.2 Overall incidence of postoperative nausea and vomiting in this study:

The 61 patients who underwent a total abdominal hysterectomy with general anesthesia in King Chulalongkorn Memorial Hospital completed this study in one year. The overall incidence of PONV in this study is 64.5% within 24 hours after the operation, which was different from the rate (80%) we got from other references for calculating sample size and affected the study power for the conclusion. The patients who suffered from PONV in the control group was 64.5% compared with the acupoint group, which was 56.7%.

5.3 Primary outcome analysis

Table 5.4 shows that the difference in the primary outcome in the two groups was not statistically significant.

The proportion of complete response in the acupoint group was greater (43.3%) than the proportion of complete response in the control group (35.5%). The difference between the proportions of the two groups with complete response was 7.8%. It is

necessary to compare the 95% Confident Interval (95% CI) of the proportional difference between the two groups.

The standard error of the proportion difference is $SE = \sqrt{P_1 q_1/n_1 + P_2 q_2/n_2}$

So the 95%CI for the true difference ranges from:

Lower limit = 0.078 – 1.96 × 0.126 = - 0.167

Upper limit = 0.078 + 1.96 × 0.126 = 0.323

So this 95% confidence interval ranged from – 16.7% to 32.3%, which included 0 means the complete response in both groups are not statistically significantly different.

Table 5.4

The analysis of two groups for complete response

Primary outcome		Acupoint group n=30	Control group n=31	Proportion difference
Complete response (%)	Yes	13/30 (43.3%)	11/31 (35.5%)	43.3% - 35.5%=7.8%
	No	17/30 (56.7%)	20/31 (64.5%)	

* Using 2x2 tables, since no cell (0%) has expected count less than 5, the minimal count is 11.8 , so Chi-square test was used for complete response rate statistical test .

Although the acupoint treatment group had higher efficacies in the complete response rate compared with the control group (43% VS 36%), the reduction of PONV from acupoint injection with normal saline failed to reach statistical significance in this study.

5. 4 Secondary Outcome Analysis

The distribution of nausea, retching, vomiting is shown in table 5.5. Both groups experienced a statistically significant difference in the vomiting (P = 0.024). The acupoint injection group experienced much less vomiting than the control group. All the retching

cases happened in the control group only, none in the acupoint injection group. However, there was no significant difference in nausea and rescue use between the two groups.

Table 5.5 The distribution of secondary outcome in two groups

Variable	Acupoint Group	Control Group	P-Value
Nausea : Mean (SD)	1.3 (1.66)	1.2 (1.58)	0.491
Retching: Mean (SD)	0	0.4 (1.02)	**< 0.001***
Vomiting: Mean (SD)	0.3 (0.67)	0.8 (2.1)	**0.024***
Rescue : Mean (SD)	0.8 (1.03)	0.7 (0.91)	0.626

Using Mann-Whitney U test.

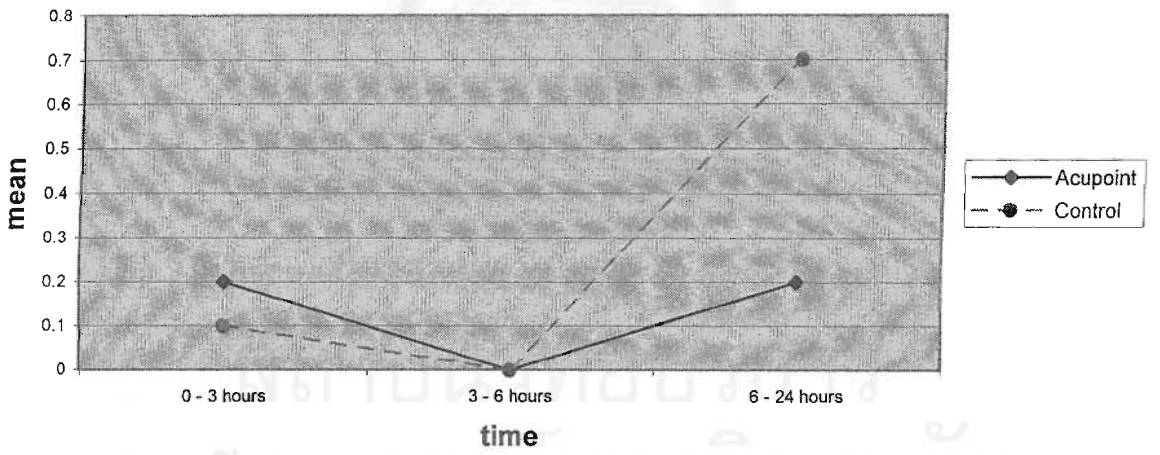
3. If we consider the difference of nausea, retching and vomiting of patients in different periods after surgery, Table 5.6 shows the retching and vomiting rate was statistically much higher in the control group than the acupoint-injection group within 6 to 24 hours significantly, all retching happened in the control group, none happened in the acupoint injection group. Fig 5.1 shows the mean of the vomiting curve changed during different periods of time between the two groups. However, there is no significant difference in the first 3-6 hours in both groups.

Table 5.6 The distribution of secondary outcome in three periods and two groups:

	Acupoint group(n=30)	Control group (n=31)	P- values
0-3 h after operation			
Vomiting: Mean(SD)	0.2(0.35)	0.1(0.3)	0.110
Retching : Mean(SD)	0	0.1(0.54)	**0.046***
Nausea : Mean(SD)	0.3(0.69)	0.2(0.76)	0.736
3-6 h after operation			
Vomiting	0	0	NA
Retching	0	0	NA
Nausea	0.4(0.77)	0.2(0.48)	0.155
6-24 h after operation			
Vomiting	0.2(0.48)	0.7(2.0)	**0.005***
Retching	0	0.3(0.89)	**0.001***
Nausea	0.6(0.77)	0.8(1.02)	0.160

* Using Mann-Whitney U test, NA = not available

Fig 5.1 The distributions of vomiting in each period in two groups



* value in vomiting is 0.005 during the 6-24 hour period after operation.

CHAPTER 6

DISCUSSION, CONCLUSION AND RECOMMENDATION

6.1 Discussion:

To date, more than three dozen randomized controlled studies have been published showing that acupoint stimulation can treat or prevent nausea and vomiting[98-103].

While most acupuncture treatments are tailored to individual patients and are highly dependent on practitioner preference points, most acupuncturists and doctors of Oriental medicine appear to prefer using the PC-6, some other Chinese papers showed using ST-36 and Liv-3 points[104].

Acupoint injection with 0.9% saline has rarely been applied to clinical studies, but much research has been applied successfully in controlling vomiting and nausea by acupuncture or acupoint injection with Chinese herbs or vitamins. Said research stated that the mechanism for reduction of nausea and vomiting with acupuncture or acupoint injection is stimulation.

The eligible 61 patients who underwent total abdominal hysterectomy under general anesthesia in King Chulalongkorn Memorial Hospital completed this study from March 2001 to April 2002. Here we used 0.9% saline for stimulation instead of medication. Although the acupoint treatment group (acupoint injection with 0.9% saline at PC-6 and ST-36) had higher efficacies in the complete response rate

compared with control group (43.3% VS 35.5%), the reduction of PONV from acupoint injection with normal saline failed to reach statistical significance under the conditions of this study. The patients who suffered from PONV in the control group are 64.5% compared with 56.7% in the acupoint group. So the difference of the two groups is only 64.5% – 56.7% = 7.8%, which is far less than our expected difference (30%). So the power is too low to detect the difference, the power of this study to detect the incidence difference is only 10%.

In addition, all the patients were blinded with psychologically positive thinking in this study, which could reduce the total incidence of PONV after a total abdominal hysterectomy from an average of 80% (from references) to 64.5% (in the conditions of this study), which also reduce the ability (power) to detect the difference of overall incidence between the two groups. Therefore, it also showed to increase the sample size could increase the power of the study to achieve justification for further conclusions.

Even though there was no difference in nausea between two groups, when the retching and vomiting are considered, the 4 cases suffered from retching during the first 24 hours only in the control group, with none in the acupoint group ($p < 0.001$). In addition, the patients who suffered more than 5 times vomiting in 24 hours were in the control group, so the frequency of vomiting was significantly less in the acupoint group compared with control group (P=0.024). Moreover, during each observation period, the third period (6-24 hours) after the operation, the acupoint injection group got much less vomiting than the control group did (P=0.005).

Those improvements may be concerned, as the influence of acupoint stimulation, while the stimulation by 0.9% saline may be not strong enough to reduce the overall incidence of PONV in this study. Moreover, we applied acupoint injection before the patients were fully alert; the nerve system did not respond properly in the first 6 hours after the operation, thus the study did not show any statistical difference between both groups, except retching. After 6 hours, study group showed less retching and vomiting compared to control group. So it is worthy of further investigation, such as prolong the observation up to 48 hours to observe the further situation.

In short, we cannot conclude that acupoint injection with 0.9% saline to stimulate PC-6 and ST-36 is an effective antiemetic for reducing overall incidence of PONV under the conditions of this study.

However, the study did show that acupoint injection with normal saline at PC-6 and ST-36 is an effective, nontoxic method to reduce numbers of retching and vomiting ($P < 0.001$ for retching and $P = 0.024$ for vomiting) in 24 hours, especially during 6-24 hours the control group had trend of increasing numbers of vomiting ($P=0.005$) after a total abdominal hysterectomy under general anesthesia. These objective outcomes are more desirable than nausea (the subjective outcome here showed no difference between two groups).

6.2 Conclusion:

In summary, this randomized double-blind controlled trial comparing acupoint with placebo group, total 61 patients who underwent a total abdominal hysterectomy under general anesthesia, and 24-hour follow up showed significant reduction of retching and vomiting, especially during the 6-24 hours after the operation. However, there was no

statistically significant difference of the overall incidence of postoperative nausea and vomiting between the two groups. Increasing sample size will increase the power of the study and prolong observation period time up to 48 hours may be able to detect more difference, since there was a trend of increasing rate of complete response in the acupoint injection group and a trend of increasing frequency number of retching and vomiting after patients fully conscious in control group.

6.3 Recommendation:

Since this study showed the average incidence of PONV was 64.5%, lower than 80% (from the reference for calculating the sample size) and the difference of incidence between the two groups is very low (7.8% instead of 30% from the high expectation for calculating the sample size) for the patients who underwent a total abdominal hysterectomy under general anesthesia in King Chulalongkorn Memorial Hospital during April 2001- April 2002, it is necessary to increase sample size to increase the power to conclude whether this treatment can effectively reduce overall incidence of PONV or not. In addition, there was a trend of increasing retching and vomiting during 6-24 hours, so prolong observational period up to 48 hours after the operation may see more difference.

If further studies can also prove the efficacy of acupoint injection with 0.9% saline for prevention and / or significant reduction nausea and / or vomiting, this low-cost, safe, non-chemical drug, no side effects and will greatly benefit patients, families, hospitals and countries all over the world. This method also can apply to any other situation, not just

postoperative nausea and vomiting, such as cancer patient after chemo or radiative therapy.

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Appendices

ข้อมูลสำหรับผู้ป่วย

การศึกษาทางคลินิก : การป้องกันอาหารคลื่นไส้อาเจียนในผู้ป่วยที่ได้รับการผ่าตัดมดลูกออกทางผนังหน้าท้อง โดยการฉีดน้ำเกลือ 0.9% ที่จุดฝังเข็ม

เรียน ผู้ป่วยทุกท่าน

ท่านเป็นผู้ที่ได้รับเชิญจากแพทย์ให้เข้าร่วมการศึกษาทางคลินิก เพื่อประเมินผลของการฉีดน้ำเกลือ 0.9% ที่จุดฝังเข็ม เพื่อป้องกันอาการคลื่นไส้อาเจียนหลังการผ่าตัดมดลูกออกทางผนังหน้าท้อง ก่อนที่ท่านตกลงเข้าร่วมการศึกษาดังกล่าว ขอเรียนให้ท่านทราบถึงเหตุผลและรายละเอียดของการศึกษาวิจัยในครั้งนี้

การผ่าตัดมดลูกออกทางผนังหน้าท้อง เป็นการผ่าตัดชนิดหนึ่งที่พบว่าโดยปกติแล้วมีอุบัติการเกิดการคลื่นไส้อาเจียนหลังการผ่าตัดสูง อันเป็นเหตุให้ผู้ป่วยรู้สึกไม่สบาย รบกวนการพักผ่อน และทำให้อาการปวดหลังการผ่าตัดของ ผู้ป่วยรุนแรงขึ้น

ตามศาสตร์ของแพทย์จีนโบราณ แนะนำว่าการกระตุ้นจุดฝังเข็ม 4 จุด ได้แก่ จุดที่ข้อมือด้านท้องแขนทั้งสองข้าง และจุดที่ขาบริเวณหน้าแข้งทั้ง 2 ข้าง สามารถระงับอาการคลื่นไส้อาเจียนได้ การวิจัยนี้จะทำให้ทราบว่าการกระตุ้นจุดฝังเข็มดังกล่าวด้วยน้ำเกลือ 0.9 % หลังจากเสร็จสิ้นการผ่าตัดและการวางยาสลบทันที จะช่วยป้องกันการคลื่นไส้อาเจียนหลังการผ่าตัดมดลูกออกทางหน้าท้องหรือไม่ ซึ่งจะช่วยทำให้ผู้ป่วยไม่ต้องทรมานหลังการผ่าตัดจากอาการดังกล่าว ไม่ปวดแผลมากขึ้นจากการอาเจียน และลดค่าใช้จ่ายสำหรับค่ายาแก้คลื่นไส้อาเจียน อันจะเป็นประโยชน์ทั้งกับท่านเองและผู้ป่วยในอนาคต

อาการข้างเคียงที่อาจเกิดจากการฉีดน้ำเกลือกระตุ้นจุดฝังเข็มดังกล่าว มีโอกาสเกิดน้อยมาก เนื่องจากเข็มที่ใช้ฉีดเล็กมาก และจำนวนน้ำเกลือน้อย เช่น อาจมีรอยช้ำและบวมเล็กน้อยที่จุดฉีดน้ำเกลือเหมือนกับการฉีดยาหรือเจาะเลือด ทั่ว ๆ ไป หากท่านมีข้อสงสัยใด ๆ แพทย์ยินดีจะตอบคำถามต่างๆ

การเข้าร่วมการศึกษานี้ เป็นไปโดยสมัครใจ ท่านสามารถปฏิเสธที่จะเข้าร่วม หรือถอนตัวจากการศึกษานี้ได้ทุกเมื่อ โดยไม่กระทบต่อการดูแลรักษาที่ท่านจะได้รับจากแพทย์

หากท่านสมัครใจเข้าร่วมในโครงการวิจัยนี้ ท่านอาจถูกสุ่มเข้าอยู่ในกลุ่มใดกลุ่มหนึ่งโดยที่ท่านเองจะไม่ทราบว่าท่านได้รับการฉีดยากระตุ้นที่จุดฝังเข็มหรือไม่ เพราะจุดดังกล่าวจะได้รับการปิดพลาสเตอร์ ท่านจะได้รับการเฝ้าดูอาการอย่างใกล้ชิด และจะได้รับการสัมภาษณ์ถึงจำนวนอาการคลื่นไส้และอาเจียนในช่วงระยะเวลา 24 ชั่วโมงหลังการผ่าตัด ทั้งนี้ท่านไม่ต้องเสียค่าใช้จ่ายใด ๆ ในการรักษาอาการคลื่นไส้อาเจียนที่อาจเกิดขึ้น

ประการสำคัญที่ท่านควรทราบคือ

ผลของการศึกษานี้จะใช้สำหรับวัตถุประสงค์ทางวิชาการเท่านั้น โดยข้อมูลต่าง ๆ จะถูกเก็บไว้ในคอมพิวเตอร์ และไม่แพร่งพรายสู่สาธารณชน ขอรับรองว่าจะไม่มีการเปิดเผยชื่อของท่านตามกฎหมาย

หากท่านมีปัญหา หรือข้อสงสัยประการใด กรุณาติดต่อ พ.ญ. เล ลี เบอร์โทรศัพท์ (01) 689-3283 ตลอด 24 ชั่วโมง หรือ พ.ญ. สุปราณี นิรุตติศาสน์ ภาควิชาวิสัญญีวิทยา ติกสิรินธร ชั้น 4 โรงพยาบาลจุฬาลงกรณ์ โทร. 0-2256-4295 ซึ่งยินดีให้คำตอบแก่ท่านทุกเมื่อ

ใบยินยอมของผู้ร่วมการศึกษา

เลขที่ผู้ป่วย..... ชื่อและนามสกุล.....

ข้าพเจ้าได้รับทราบจากแพทย์ผู้รักษา ซึ่งได้ลงนามด้านท้ายของหนังสือนี้ ถึงวัตถุประสงค์ ลักษณะและแนวทางการศึกษาการป้องกันอาการคลื่นไส้อาเจียนในผู้ป่วยที่ได้รับการผ่าตัดมดลูกออกทางผนังหน้าท้อง โดยการฉีดน้ำเกลือ 0.9% ที่จุดฝังเข็ม รวมทั้งทราบถึงผลดี ผลข้างเคียง และความเสี่ยงที่อาจเกิดขึ้น ข้าพเจ้าได้ซักถาม ทำความเข้าใจเกี่ยวกับการศึกษาดังกล่าวนี้ เป็นที่เรียบร้อยแล้ว

ข้าพเจ้ายินดีเข้าร่วมการศึกษาวิจัยครั้งนี้โดยสมัครใจ และอาจถอนตัวจากการเข้าร่วมศึกษานี้เมื่อใดก็ได้โดยไม่จำเป็นต้องแจ้งเหตุผล และยอมรับสิ่งไม่พึงประสงค์ที่อาจเกิดขึ้น และจะปฏิบัติตัวตามคำแนะนำของแพทย์ทุกประการ

ข้าพเจ้าได้รับทราบจากแพทย์ผู้รักษาว่า หากข้าพเจ้าได้รับความผิดปกติเนื่องจากการทดลอง ข้าพเจ้าจะได้รับความคุ้มครองตามกฎหมาย และหากข้าพเจ้าเข้ารับการรักษาทางการแพทย์อื่น ๆ โดยมิได้ปรึกษาแพทย์ผู้รับผิดชอบการศึกษานี้ และมิได้แจ้งให้แพทย์ทราบในทันทีถึงความผิดปกติของร่างกายที่เกิดขึ้นได้จะถือว่าข้าพเจ้าทำให้การคุ้มครองความปลอดภัยเป็นโมฆะ (ตามที่กฎหมายกำหนด)

ข้าพเจ้ายินดีให้ข้อมูลของข้าพเจ้าแก่คณะแพทย์ผู้รักษา เพื่อเป็นประโยชน์ในการศึกษาวิจัยครั้งนี้

สุดท้ายนี้ ข้าพเจ้ายินดีเข้าร่วมการศึกษานี้ ภายใต้เงื่อนไขที่ได้ระบุไว้แล้วในข้างต้น

....

( )

สถานที่/วันที่ ลงนามผู้ป่วย

....

( )

สถานที่/วันที่ ลงนามแพทย์ผู้ให้การรักษา

....

( )

สถานที่/วันที่ ลงนามพยาน

Data collection form

Acupoint Injection for prevention of PONV

Hospital No..... Code No.....

Date of information:.....

A. Baseline data :

1. Name.....
2. Age.....years
3. Height.....(cm)
4. Weight.....(kg)
5. Last menstrual cycle.....
6. Migraine (severe headache along with nausea or vomiting) [ ] 1. Yes, [ ] 2. No,
7. Motions sickness [ ] 1. Yes, [ ] 2.. No,
8. History of previous disease.....
9. History of drugs allergy : .....
10. Current medications : .....
11. History of Post Operative Nausea and Vomiting (PONV) [ ] 1. Yes, [ ] 2. No,
12. Blood pressure before operation.....mmHg
13. Pulse before operation...../min.
14. Duration of surgery.....hours and.....min. operation finished at.....
15. Duration of anesthesia.....hours and.....min.
16. Anesthesia drugs, some may cause PONV :

    Midazolam.....mg, Succinycholine.....mg, Thiopental.....mg,

    Nitrous oxide.....%, Isoflurane.....%, Fentanyl.....ug,

    Vecuronium..... instead of using Pavulon.....mg,

    Physostigmine.....mg, Atropine.....mg

    Others :

B. Outcomes :

Primary :

1. Complete response (no nausea, no retching, and no vomiting). [ ] 1. Yes, [ ] 2. No.

Secondary :

2. Nausea [ ] 1. No. [ ] 2. Yes. Nausea Score = NS

.....times/0-3h, Highest NS = ...

.....times/3-6h, Highest NS = ...

.....times/6-24h, Highest NS = ...

Nausea Score (NS) 0.....10

No severe

Total :.....times/24 hours. The highest nausea score...../24 hours

3. Retching [ ] 1. No, [ ] 2. Yes,

.....times/0-3h, ...times/3-6h, ...times/6-24h.

Total : .....times/24 hours.

4. Vomiting [ ] 1. No, [ ] 2. Yes,

.....times/0-3h, ...times/3-6h, ...times/6-24h.

Total : .....times/24 hours.

5. Rescue antiemetics : [ ] 1. No. [ ] 2. Yes.

[ ] Metoclopramide (0.15 mg/kg) .....times/24 hours.

Injection 1. .....mg. Time .....

Injection 2.....mg. Time .....

[ ] Ondansetion (0.08 mg/kg).....times/24 hours.

Injection 1. .....mg. Time .....

Injection 2.....mg. Time .....

6. Adverse effects [ ] 1. No,

[ ] 2. Pain, [ ] 3. Hematima, [ ] 4. Neuritis.

[ ] 5. Others. (please specify).....

15. Duration of opioid used after operation.....hours.

Morphine.....mg/24 hours.

ระดับความคลื่นไส้ (Nausea Score = NS)

ชื่อ..... **นามสกุล**..... Code.....

0-3 ชั่วโมง = ... **3-6 ชั่วโมง** = ... **6-24 ชั่วโมง** = ...

ระดับความคลื่นไส้ (Nausea Score = NS) **ถ้า > 4 ให้ยารักษาคลื่นไส้อาเจียน**

Retching [ ] 1. No, [ ] 2. Yes,

.....times/0-3h, ...times/3-6h, ...times/6-24h.

Total : .....times/24 hours.

Vomiting [ ] 1. No, [ ] 2. Yes,

.....times/0-3h, ...times/3-6h, ...times/6-24h.

Total : .....times/24 hours.

Rescue antiemetic : [ ] 1. No. [ ] 2. Yes.

[ ] Metoclopramide (0.15 mg/kg) .....times/24 hours.

Injection 1. .....mg. Time .....

Injection 2.....mg. Time .....

[ ] Ondansetion (0.08 mg/kg).....times/24 hours.

Injection 1. .....mg. Time .....

Injection 2.....mg. Time .....

1). เวลา..... NS.....

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0 10

2). เวลา..... NS.....

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0 10

3). เวลา..... NS.....

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0 10

4). เวลา..... NS.....

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0 10

VITAE

Dr. Li Lei was born on December 17, 1962 in Kunming, Yanna, and P.R. China. She graduated from Kunming Medical College, Yanna, and P.R. China in 1984. After graduation, she worked at First Teaching Hospital, Kunming Medical College as a doctor and a teacher for postgraduate students in Nuclear Medicine for over ten years. During her clinical practice, she worked in nuclear medicine; in part time she also studied, practiced and did research in Traditional Chinese Medicine. Since June 1999, she has been working in the Master Degree Program of Health Development in the Faculty of Medicine of Chulalongkorn University, Bangkok, Thailand.

Her principle interest in the medical field is using the scientific method to prove Traditional Chinese Medical theory and research in combination with Western Medicine for treating medical disorders. Trying to build a bridge between Traditional Chinese Medicine and Western Medicine in order to take the advantages and avoid the disadvantages of both medicines. During this course, she has conducted a clinical trial on the effect of acupoint injection for the prevention of postoperative nausea and vomiting after a total abdominal hysterectomy at King Chulalongkorn Memorial Hospital, Bangkok, Thailand.

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