An-Najah National University

Faculty of Graduate Studies

PREVENTING POSTOPERATIVE NAUSEA AND VOMITING IN FEMALE PATIENTS HAVING LAPAROSCOPIC CHOLECYSTECTOMY SURGERY WITH METOCLOPRAMIDE ALONE VS. METOCLOPRAMIDE COMBINED WITH P-6 ACUPRESSURE STIMULATION

By

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This Thesis is Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Nurse Anesthesia, Faculty of Graduate Studies, An-Najah National University, Nablus - Palestine.

2024

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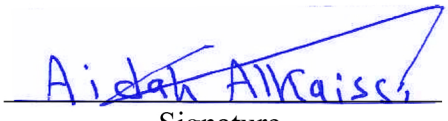
Dr. Aidah Alkaissi	
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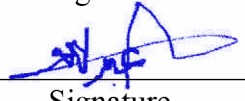
Dr. Abdallah Alwawi	
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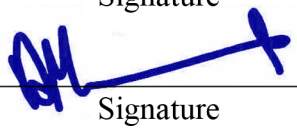
Dr. Mohammed Jaber	
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Dedication

I dedicated this thesis to the sake of Allah, and my great teacher and messenger, Mohammed (May Allah bless and grant him), who taught usthe purpose of life.

To my homeland, Palestine, the intimate womb, and to the great martyrs and prisoners, the symbol of sacrifice.

My great parents, who have always loved me unconditionally and taught me to work hard for the things that I aspire to achieve, are my beloved sister and brothers. I dedicate this research to all my family and friends who encourage and support me and all the people in my life who touch my heart.

Acknowledgements

First, I give all the glory to God, the source of my strength, for granting meboth the mental and physical endurance to complete this monumental task.

I would like to extend a very special thanks to my advisor Dr. Aidah Alkaissi, for believing in me and for their diligent supervision, clear guidance, continued support and encouragement throughout this process.

Then, I would like to thank my entire family, especially my loving parents, for their love, support, and encouragement during graduate school and life challenges.

Thank you to everyone who gave me moral support for completing this task.

Declaration

I, the undersigned, declare that I submitted the thesis entitled:

PREVENTING POSTOPERATIVE NAUSEA AND VOMITING IN FEMALE PATIENTS HAVING LAPAROSCOPIC CHOLECYSTECTOMY SURGERY WITH METOCLOPRAMIDE ALONE VS. METOCLOPRAMIDE COMBINED WITH P-6 ACUPRESSURE STIMULATION

I declare that the work provided in this thesis, unless otherwise referenced, is the researcher's own work, and has not been submitted elsewhere for any other degree or qualification.

Student's Name: **Dana Ewesat**

Signature: 

Date: **14/11/2024**

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Abstract

Evidance suggests the possible importance of non-pharmacological treatments in preventing PONV in high-risk patients due to no antiemetic that is effective in lowering PONV despite extensive research. In order to prevent PONV in female patients undergoing laparoscopic surgeries under general anaesthesia, this study examines the efficacy of metoclopramide both alone and in combination with P-6 acupressure. In contrast, the first randomization occurs on the day of the surgery and determines whether metoclopramide will be used as a standalone measure of antiemetic pharmacotherapy.

One hundred sixteen female patients were divided into four groups in a rigorous prospective, randomized, double-blind, placebo-controlled trial. The Combination group (n = 28) received P-6 acupressure 30 minutes before anaesthesia induction as well as 10 mg of metoclopramide immediately before anaesthesia induction; the Acupressure group (n = 30) received P-6 acupressure and 1 ml of NaCl; the Pramin group (n = 29) received 10 mg of metoclopramide and placebo acupressure; the Placebo group (n = 29) received placebo acupressure and 1 ml of NaCl. Postoperative symptoms were assessed during the next 24 hours.

There were significant differences ($p < 0.001$) in the incidence of vomiting within 24 hours after surgery between the Combination 44.3%, Acupressure 20%, Pramin 11.9%, and Placebo group 17.6. %. A statistically significant difference was found between the Combination and Placebo groups as well as the Combination and Pramin groups as Post Hoc test identificate. There is evidence that a significant difference in nausea within 24 hours after surgery was found in Acupressure 26.7 % and Combination 17.9 % compared to Placebo group 62.1 %, p-value < 0.05. Only 24 hours after surgery, there were notable

variations in the severity of nausea between the Combination (0.17) and the Placebo (0.81), with a p-value of 0.006. In the entire 24-hour period, compared to Placebo 51.7%, combination 14.3%, and Acupressure group 23.3% have significantly lower usage rates of rescue antiemetic, $p < 0.05$.

In female patients undergoing laparoscopic surgery, metoclopramide plus bilateral P-6 acupressure significantly reduces PONV as well as the need for rescue medication, making it a stronger preventive approach than either medication alone.

Keywords: Laparoscopic Cholecystectomy; Metoclopramide; Non-Pharmacological Therapies; P-6 Acupressure; Postoperative Nausea and Vomiting (PONV).

Chapter One
Introduction

1.1 Introduction

Research on nausea and vomiting has been carried out for a long time. Recent theoretical developments have revealed that postoperative nausea and vomiting remain one of the utmost stressful adverse effects and primary contributor during the postoperative period, even greater than postoperative pain (Ahn et al., 2016; Uemura et al., 2019). Scholars defined it as an experience of nausea, retching, or vomiting in patients within the first 24-48 hours post-surgery (Hijazi et al., 2018).

The pervasiveness of PONV is between 20%–30% in normal populations and up to 70% –80% in high-risk people, especially in strabismus, tonsillectomy, and laparoscopic surgeries (Amirshahi et al., 2020). Hence, evaluating PONV is noteworthy because it is one of the biggest complications that can lead to morbidity through postponed postoperative healing by causing electrolyte imbalance, dehydration, pulmonary aspiration suture dehiscence, and pneumonia, so if severe enough, oesophageal rupture (Elsaid et al., 2021; Joo et al., 2022). The aspects can generally be separated, starting with patient aspects, surgical aspects, pharmacological aspects, anaesthetic techniques, and post-operative care factors. With this in mind, PONV is a multi-factorial problem (Shrestha et al., 2019). It's important to realize that many aspects affect PONV, such as sex, age, smoking, surgical procedure, and patient and parental anxiety (Kampmeier et al., 2021).

Because there is no exclusive one antiemetic drug that has been authorized to be a global solution (Kumar et al., 2013), surgeons and anaesthetists prefer to use a combination of antiemetic medications to diminish PONV versus one-shot agent treatment, particularly for high-risk patients (Bilgen et al., 2018). Despite further advances in prophylactic drugs for PONV treatment, the occurrence is still rather high. Therefore, extra non-pharmacological medications are required (Nowak et al., 2022), such as acupressure due to increasing the release of β-endorphins from the hypothalamus into the cerebrospinal fluid, along with modulating serotonin transmission via serotonergic and norepinephrinergic system mechanisms which play important role in PONV (Stoicea et

al., 2015), According to a study on P6 acupoint stimulation, it is a great supplement to antiemetic medication therapy for the successful prevention of PONV so study of combination of dexamethasone and TEAS of P6 has a better effect on PONV prophylaxis than dexamethasone alone, and it is comparable to the combination of tropisetron and dexamethasone (Oago & Alapiha, 2023).

Based on the brief review above, this study mainly aims to assess the effect of metoclopramide alone vs in Combination with P-6 Acupressure stimulation for PONV in female patients.

1.2 Problem Statement

Post laparoscopic cholecystectomy, high rates of postoperative nausea and vomiting were noted due to peritoneal insufflation with carbon dioxide gas so the pathway is the activation or stimulation of the chemoreceptor trigger zone, through the activation of serotonin receptors in the gut with another contribute factors such as a history of motion sickness, stress type personalities, young females, non-smokers, and general anesthesia (Ahmad et al., 2023). The figures are as follows: 55.8% for the second-hour post-surgery, 41.9% for the sixth hour, 30.8% for the twelfth hour, and 11.6% for the twenty-fourth hour. These rates are notable even though laparoscopic surgery is typically associated with fewer complications compared to open surgery, with few medical and anaesthetic problems associated with a large incision (Yayla et al., 2022). PONV is linked to enhanced unplanned hospitalization and postponement of discharge from the postanesthesia care unit. The situation increases medical costs in patients and hospitals (Elvir-Lazo et al., 2020). Therefore, the study aimed to evaluate the effect of prophylactic metoclopramide on postoperative nausea and vomiting in female patients who have been through laparoscopic cholecystectomy, both as monotherapy and in combination with P-6 acupressure stimulation. As evidenced of combination pharmacological antiemetic such as ondansetron or dexamethasone with acupressure P6 wristband significantly reduced the incidence of PONV and the need for rescue anti-emetics when compared with the single antiematic (Trueman, 2011; Zhong et al., 2023). Four groups were randomly assigned to 120 female patients, who were ASA physical status I and II, and ranged in age between 18 and 65. Under general anaesthesia, these groups' therapies were evaluated for their efficacy in treating individuals who were determined to be at a moderate to high PONV risk.

1.3 Background

1.3.1 Definition and Pathophysiology of Nausea and Vomiting

Post-operative nausea and vomiting are common adverse reactions that occur in patients having surgery under general anaesthesia (Elsaid et al., 2021). The definition of nausea is a private, undesirable sensation that cannot be measured by the observer, only by the individual, so The sensation is best characterized as wanting to throw up without actually moving the stomach muscles violently (Apfel et al., 2002) . Vomiting is an opening of the cardiac sphincter due to a strong diaphragmatic and abdominal muscular contraction. Vomiting is a forceful expulsion of gastric contents through the mouth (Apfel et al., 2002). On the other hand, retching is contractions of the respiratory muscles that are rhythmic and spasmodic. It also usually involves the chest wall, the diaphragm, and abdominal wall muscles, but there is also a type of procedural retching that does not smell and produces nothing. It may also be mouth-opening without expulsing the gastric content (Watcha & White, 1992). Hence, it can be described as something that happens once the stomach has been evacuated. It is also usually not an experience that a patient would like to repeat. This episode is usually followed by an emetic episode (Apfel et al., 2002).

The "vomiting centre," an ill-defined neuroanatomical location within the lateral reticular formation of the medulla that is activated by CNS stimuli from a variety of sources, such as the cerebral cortex, the vestibular system, the enteric vagal nerve afferents, and the chemoreceptor trigger zone (CTZ), is the neuroanatomical location responsible for controlling nausea and vomiting (Shaikh et al., 2016).

The chemoreceptor trigger zone is situated in the postrema region of the fourth ventricle, close to the emetic centre, and beyond the blood-brain barrier. It includes mu, dopamine type 2 (D2), cholinergic muscarinic (M1), serotonin 5-hydroxytryptamine type 3 (5HT3), and substance P neurokinin type 1 (NK1) receptors are among them (Maharjan & Bing, 2021; Stoops & Kovac, 2020).

Additional interactions develop with the nucleus tractus solitaries in the fourth ventricle floor containing high 5HT3, mu, and NK1 receptors. Cholinergic (M1), histamine H1, and muscarinic (M3 and M5) receptors are located within the vestibular (Stoops & Kovac, 2020).

Various substances, including drugs and electrolytes, can activate the receptors that trigger vomiting. The antiemetic drugs used for PONV also block these different neurochemical receptor sites, which causes stimulation to be delivered to the vomiting centre and establishes the vomiting reflex. This helps explain why, in certain high-risk patients, a combination of different antiemetic therapies may be necessary (Doubravska et al., 2010).

Laparoscopic and intraabdominal surgery have been linked to a higher incidence of PONV.due to an increase of intraabdominal pressure that manipulates the stomach and GI tract through the head-down Trendelenburg position or insufflation of the abdomen (Lingle, 2019; Stoops & Kovac, 2020). The gut, oropharynx, pain, hypoxemia, and hypotension may also trigger the vomiting centre. Thus, the vomiting centre is stimulated, and the efferent signals move via the glossopharyngeal, hypoglossal, trigeminal, accessory, and spinal segmental nerves (Lingle, 2019). The vagus nerve is the main nerve responsible for perceiving and navigating emetic cues originating from the gastrointestinal tract (Stoops & Kovac, 2020).

1.3.2 Risk Factors

It remains one of the most persistent adverse reactions in patients regarding anaesthesia/surgery. It delays discharge and impairs the quality of care and the possibility of resuming daily activities (Maharjan & Bing, 2021). In addition to risk factors and Types of Procedures, Apfel simplified their risk score to include female sex, history of motion sickness or PONV, non-smoker status, and requirement for postoperative opioid menage. To help identify patients that may receive benefits. With this in mind, the risk of PONV should be assessed based on 3 sets of Patient Anesthesia and surgery-related risk factors (Apfel et al., 1999).

- **Anesthesia-Related Risk Factors**

A series of recent studies indicated that anaesthetics have several risk factors. These risk factors include volatile anaesthetics and intravenous agents. An increase in the duration and concentration of volatile anaesthesia will lead to increases in the incidence of PONV, particularly in the preliminary postoperative phase of 2-6 hours. In addition, there is no difference between any volatile anaesthesia and the incidence of PONV. It depends on

duration and concentration (Maharjan & Bing, 2021). According to recent research, the incidence of PONV is increased by nitrous oxide and large dosages of neostigmine used to reverse residual neuromuscular blockade (Elvir-Lazo et al., 2020).

In high-risk cases, using an opioid-free approach is effective in reducing PONV (Massoth et al., 2021). In addition, a reduction of opioid dose to half declines the incidence of PONV by 6% (Maharjan & Bing, 2021). For instance, the administration of a long-acting compound rather than a short-acting opioid can serve as a possible PONV risk factor (Gan, 2006). On the one hand, propofol can present antiemetic effects because it produces synaptic transmission declines in the olfactory cortex. A probably correct answer is that it follows with declines in aspartate and glutamate release, which are the first things set off during radiation in terms of emesis. However, propofol seems to have a high degree of correlation with nausea and vomiting. It may decrease the release of various central substances, which probably follows with declines in the deglutitive central nuclei in the medulla and likely decrease the vagal nuclei and the CTZ (Lingle, 2019).

Increasing the length of surgery is a separate risk factor for PONV, so a thirty-minute increase in operating time could result in a 60% increase in PONV risk (Shaikh et al., 2016).

- **Age**

The incidence of PONV is low in paediatrics under three years old, and it increases in schoolhood time by 34-45%. For those aged <50 years, the incidence decreases by 13% for the addition of each 10 years of age (Maharjan & Bing, 2021).

- **Female Gender**

The higher incidence of PONV in women is three times more than in males. This may be linked to fluctuating female hormones during the menstrual cycle (Maharjan & Bing, 2021) due to follicle-stimulating hormone and estrogen release. PONV may be attached to the pre-ovulatory phase (Hambridge, 2013).

- **Smoking**

Nonsmokers are more prone to PONV twice than smokers (Maharjan & Bing, 2021; Shaikh et al., 2016). Tobacco smoke's anti-emetogenic properties may decrease the receptor's response to receptors in the CNS, leading to PONV. Moreover, smoking plays a role in increasing the ingestion of volatile agents and opioids as well as increasing the activity of CYP1A2 and CYP2E1 enzymes (Stoops & Kovac, 2020).

- **History of PONV**

Patients with a previous history of postoperative nausea and vomiting are three times more likely to experience nausea and vomiting during general anaesthesia (Maharjan & Bing, 2021). Susceptibility to motion sickness occurs when the histamine H1 and muscarinic M2 receptors in the vestibular system are activated (Stoops & Kovac, 2020).

- **Genetics**

The idea of family history of PONV, which was discovered to be a significant risk factor in pediatric patients, initially provided evidence for the contribution of individual genetic susceptibility to PONV, so observations and the understanding that serotonin acts as a pro-emetic and antagonists of 5-HT3 type (such as ondansetron) are useful as anti-emetic therapy led to some researches about the polymorphisms that influence some of the genes encoding serotonin receptors and their association with nausea and vomiting, some evidence have found correlations between HTR3A and HTR3B polymorphisms and PONV, Genetic changes caused by other serotonin receptors such as 5-HTR2A, might also be involved in PONV development, Other mutational changes which were found to be significantly related with nausea and vomiting were in the type 2 dopamine receptor (DRD2), neurokinin-1 receptor (TACR1), type 3 muscarinic acetylcholine receptor (CHRM3) and the cathechol O-methyltransferase (COMT) gene which is involved in catecholamines degradation (Gloor et al., 2022) .

- **Weight**

Adipose tissue in obese patients raises the risk for PONV more than in nonobese patients due to the accumulation of more volatile anaesthetic in adipose tissue, which in turn aggravates PONV. In addition, They have a greater stomach volume, are more likely to experience gastric oesophageal reflux disease, and are more likely to suffer from liver and

gastrointestinal disorders, which increases the incidence of PONV (Maharjan & Bing, 2021).

- **Laparoscopic Surgeries**

Both laparoscopy and gynaecological surgery have been independent risk factors for PONV (Massoth et al., 2021). Its incidence following laparoscopic cholecystectomy is higher, between 45 and 75%, due to pneumoperitoneum in laparoscopic cholecystectomy that increases the vagal discharge (Sridharan & Sivaramakrishnan, 2019). It can be understood that the gas used to "inflate the abdomen to create a workspace for the instruments," which exerts pressure on the vagus nerve, which has been connected to the centre for nausea and vomiting, could be the cause of the high rate of PONV during laparoscopies (Tuna et al., 2017).

1.3.3 Pharmacological Risk Factor

An excellent antiemetic regimen for adults and children in the surgical setting has not yet been well-established (Cao et al., 2017). Moreover, multimodal antiemetics with different techniques offer complementary advantages, each of which lowers the relative risk of PONV by roughly 25% (Ma et al., 2022).

Unfortunately, the Combination of four prophylactic antiemetic interventions cannot decrease the incidence of postoperative nausea and vomiting with certainty beneath 10% in high-risk patients with a baseline risk between 60% and 80% (Kranke et al., 2020).

- **Metoclopramide**

Metoclopramide is considered a peripheral and central dopamine-2 receptor (D2) antagonist in the medullary chemoreceptor trigger zone in the postrema region and inhibits the central dopamine receptor, which is often triggered by levodopa or apomorphine. Extrapyramidal side effects can be unfavourable reactions, as well as headache, drowsiness, and sedation effects. However, a 10mg metoclopramide dose is considered safe and shows no extrapyramidal side effects (De Oliveira Jr et al., 2012; Maharjan & Bing, 2021). Metoclopramide is an agonist at 5HT4 and an antagonist at 5HT3 (type 3 serotonin receptors) receptors (Isola et al., 2024). Metoclopramide has a gastrokinetic impact by raising the gastrointestinal tract's selective cholinergic response

and inhibiting the relaxation of the stomach's smooth muscle. This increases the tone of the lower oesophagal sphincter and lowers the risk of aspiration (Kaur et al., 2019).

1.3.4 Non-Pharmacological Treatment

Significantly, researchers sought to determine the potential benefits of non-pharmacologic therapies, such as acupuncture, acupressure, and transcutaneous electrical nerve stimulation. On the negative side, pharmacologic interventions have inevitably failed to combat PONV and contain emetic episodes or decrease side effects. In addition, it is important to note some of the study's limitations, such as the idea that the therapy might lack individual sessile effects that were not accounted for in the research (Elvir-Lazo et al., 2020).

Non-pharmacological methods are the most effective in preventing PONV, reducing the incidence of dizziness and pruritus, and reducing the number of patients who required antiemetic rescue, a helpful strategy for improving recovery, postoperative analgesia, patient satisfaction, and speeding up discharge (Oago & Alapiha, 2023).

- **P6-Acupressure**

By applying pressure on the P6 point, also known as Neiguan, it is possible to alleviate nausea and vomiting, relieve chest and abdominal congestion, relax the mind, and lessen feelings of excitement and motion sickness. It is located between the long flexor tendons on the medial surface of the forearm, three finger-widths up from the wrist crease, approximately 6 cm proximal to the wrist (Jin et al., 2020; Mobarakabadi et al., 2020), also it indicates that it is an excellent adjunct to antiemetic drug (Oago & Alapiha, 2023).

A quasi-experimental study with pre-and post-test control group design was conducted on 64 respondents to determine the effectiveness of Acupressure in decreasing Postoperative Nausea and Vomiting after general anaesthesia. They were grouped with ASA physical status I and II, BMI 18-25 kg/m 2, aged 18-45 years old, and an Aldrete score ≥8. The Gordon observation sheet nausea score was used for comparison in the control and intervention groups. In the intervention group, Acupressure was done by the right or left hand, whichever was not attached to an injury or infusion, bruised, swollen, or broken. Nausea and vomiting were reassessed 30 minutes after the Acupressure administration. The outcomes demonstrated a significant difference between the

intervention group's (p=0.000) and the control group's (p=0.057) nausea and vomiting responses before and after acupressure (Ratnawati & Muntholib, 2019).

In a randomized clinical trial, patients were randomly divided into two groups: the 43 patients in the intervention group received wrist acupressure. In the control group comprising 41 patients, the band was applied at the wrist, and the beads were put instead on the dorsal surface; the beads were placed exactly on the P6 point. The acupressure was given to patients from both groups before the onset of anaesthesia, during an intraoperative period, and after for six hours; it should be considered that patients were asked to undergo the laparoscopic cholecystectomy. There was no change in PONV after 30 minutes, 3 hours, and 6 hours after surgery in the PACU among patients from the control and intervention groups. Furthermore, both groups received equal doses for rescue antiemetics (P=0.744) (Hamid et al., 2022).

Insignificant difference between the ondansetron 0.15 mg/kg IV group and the P-6 Acupressure group, even though both groups have taken dexamethasone 0.15 mg/kg IV intraoperatively, regarding the number of patients experiencing nausea and vomiting or the intensity of vomiting in 80 patients following elective laparoscopic colorectal surgery within the first 24 hours following operation (Rehman et al., 2022).

1.4 Literature Review

In this section, the researcher presents the literature related to the study's topic. In the first place, the researcher used the PubMed, Google Scholar, and Sci-hub databases to search for PONV-related articles, using the keywords: PONV; laparoscopic; cholecystectomy; metoclopramide; P-6 Acupressure.

The gold standard approach for cholecystectomy is laparoscopy (Pucher et al., 2018), and 60% of laparoscopic cholecystectomy are performed in an ambulatory regimen in the United States and up to 78% in the United Kingdom in daycare (Manzia et al., 2020).

Unfortunately, the lack of a clear onset stimulus and the variety of potential etiologies make it difficult to determine the true incidence of PONV (Kalyani Bala et al., 2022). For all surgical procedures performed under general anaesthesia without the use of antiemetic medication, the incidence of PONV is approximated to be between 25% and 30%

(Sridharan & Sivaramakrishnan, 2019) including laparoscopic cholecystectomy, which has an incidence rate between 40% and 75% greater than other surgical procedures in individuals who did not get antiemetic therapy following the procedure (Bameshki et al., 2018; Kalyani Bala et al., 2022).

A random assignment was done to place 120 female patients who had undergone laparoscopic surgery and were at a moderate-to-high risk of PONV into one of four groups without informed consent: the 20 mg metoclopramide group, the 8 mg dexamethasone group, the 8 mg dexamethasone with a 20 mg metoclopramide group. The patients in the Combination group 6 (20%), Placebo group (17) (56.7%), and dexamethasone group 6 (20%) all experienced significantly different rates of vomiting than the placebo group, which received saline. In comparison to Placebo 19(63.3%), there was statistically significant variation in incidences of nausea in the treatment groups, and they are dexamethasone 6(20%), metoclopramide 10(33.3%) and Combination 5(16.7%). This implies that all treatment groups generally have similar effects in terms of reducing the incidences of nausea. The mean and standard deviation of the nausea levels experienced by the dexamethasone 1.78 (± 1.14) and combination group was 1.05 (± 0.90), P = 0.008. In the placebo group 3.07 (± 1.34), P = 0.000 and the dexamethasone and 2.43 (± 1.03), P = 0.000. According to the results, the Combination can significantly reduce the level of nausea. Compared to those getting a placebo, those receiving rescue antiemetic in dexamethasone 7 (23.3%) and Combination 6 (20%) were substantially lower than Placebo 19 (63.3%), $p < 0.05$ (Alkaissi et al., 2017).

Three groups of seventy-two patients, both male and female, undergoing laparoscopic cholecystectomy or open appendectomy were randomly assigned equally. Groups received 8 mg of dexamethasone, 100 ml of regular saline, and 10 mg of metoclopramide. Regarding nausea and vomiting, the results were not statistically different from those of the dexamethasone and normal saline groups. Comparing the metoclopramide group with the dexamethasone group and the metoclopramide group with the normal saline group also reveals a noteworthy difference. Patients in the dexamethasone group reported less discomfort than those in the normal saline and metoclopramide groups, respectively ($p < 0.01$ and $p < 0.0001$). In addition, patients in the normal saline group reported less pain ($p < 0.0001$) than those in the metoclopramide group. These findings suggest that

dexamethasone is more effective in reducing PONV than metoclopramide, and its effects are superfluous in the normal saline group. However, when compared to normal saline and metoclopramide, dexamethasone is more effective in reducing pain (Al-Radeef et al., 2020).

In a prospective randomized, double-blind, placebo-controlled study, there were no significant differences in the incidence of PONV within a 24-hour period when performing metoclopramide, ondansetron, and acupressure. However, metoclopramide 0.2mg/kg IV, ondansetron 0.15 mg/kg IV, and acupressure at P6 led to a significant reduction in the incidence of PONV 24 hours after patients aged 10-60 years old undergoing strabismus surgery (Ebrahim Soltani et al., 2011).

A study of randomized control trial showed that the non-pharmacological method of P6 Acupressure could effectively be used to reduce early postoperative nausea and vomiting, same as dexamethasone and metoclopramide in early postoperative period for 59 adult female patients underwent laparoscopic cholecystectomy which 16% of group p- 6 Acupressure bilateral and 14.8% of group dexamethasone 8 mg + metoclopramide 10 mg iv complained from nausea in first hour after recovery. At 3rd hour, 12% of group p- 6 Acupressure bilateral and 7.4% of another group complained of vomiting with insignificant differences between study groups in Bellville score. Patients having a Bellville score greater than two were treated with ondansetron 4 mg intravenously as a rescue antiemetic (Mohsin et al., 2022).

The common pharmacological treatments are costly, have potential side effects (Roehrich, 2016), and are considered partially effective (Hirš et al., 2013). In contrast, P-6 Acupressure is an anaesthetist with a safe mechanism and is cost-effective in reducing PONV (Roehrich, 2016).

One group was given bilateral P6 acupressure, n = 139 were treated with equivalent pressure to bilateral non-acupressure sites, and one control group, n = 136, was established. PONV decreased significantly from 46% to 33%. The difference was statistically significant as the test showed that PONV was identified in 46% of the standard group, 38% after triggering a non-acupoint, and 33% after P6 Acupressure. Additionally, “P6 Acupressure” in a consecutive, randomized, multicenter, placebo-

controlled, double-blind clinical trial conducted in a patient undergoing elective gynaecological surgery under general anaesthesia, did not differ substantially from Non-Acupoint Pressure, P = 0.1659 (Alkaissi et al., 2002).

For this quasi-experimental study with a pretest and posttest and a control group design, two groups of 64 participants were formed. The study aimed to establish the effects of acupressure on post-operative nausea and vomiting during general anaesthesia. Ages 18 to 45 years, ASA I and II; BMI: 18 to 25 kg/m2, Aldrete score ≥8. calculating the nausea scores for the comparison and intervention groups using Gordon's observation sheet. After 30 minutes of administration, the intervention group's right or left hand, which was not connected to the infusion or hurt, was swollen, bruised, or broken was reassessed for nausea and vomiting and used for acupressure. The outcome demonstrated a statistically significant difference between the intervention group (p = 0,001) and the compression group (p = 0.057) in terms of the occurrence of nausea and vomiting responses before and after acupuncture (Ratnawati & Muntholib, 2019).

In patients who are at high risk of developing postoperative nausea and vomiting (PONV) following laparoscopic cholecystectomy, a study was done to evaluate the effects of Acupressure on the P6 acupoint utilizing wristbands. Three groups of 111 female individuals participated in the trial. A cap was given to Group 1 at the P6 acupoint. Group 2 was given an identical-looking placebo wristband without a cap. Group 3 served as the control group. The incidence of nausea between two and six hours after surgery was greatly reduced, and the severity of nausea during the second postoperative hour was significantly lessened (P > 0.05) when the Acupressure wristband was applied at the P6 acupoint. Nonetheless, no statistically significant distinction between the control and intervention groups was found. As a result, it was determined that acupressure on the P6 acupoint was not clinically useful in reducing the need for antiemetic medicine, pain, anxiety, or analgesic drugs or in limiting postoperative vomiting P > 0.05 (Sahin et al., 2018).

Ninety patients, ages 20 to 60, with ASA I and II ratings, had middle ear surgery under general anaesthesia in a prospective, randomized, double-blind clinical trial. The patients were split into two groups: group A, which included 45 patients, received acupressure on the P 6 pressure point, and group B, which also included 45 patients, received ondansetron

following endotracheal intubation at a dosage of 0.1 mg/kg. The authors came to the conclusion that P 6 acupuncture reduces postoperative nausea and vomiting (PONV) almost as well as ondansetron. This conclusion was drawn from data that revealed no discernible variation in the frequency of nausea and vomiting between the two groups every six hours throughout a 24-hour period, with a p-value of more than 0.05 throughout all time intervals (Kumar, 2017).

1.5 Significance of the Study

The overall incidence of postoperative nausea and vomiting (PONV) is today estimated to be between 25 and 30 per cent, despite notable advancements in the field and the advent of contemporary antiemetic medications. For patients who were untreated and had multiple known risk factors, the rate might reach 80% (Stoops & Kovac, 2020).

Postoperative nausea and vomiting are the greatest common complaints post regional, local, or general anaesthesia. They can lead to morbidity through delayed postoperative healing by causing electrolyte imbalance, dehydration, metabolic alkalosis, pulmonary aspiration, incisional hernias, suture dehiscence, pneumonia, and, if severe enough, oesophagal rupture (Shrestha et al., 2019).

Respectively, 10%, 21%, 39%, 61%, and 79% are the incidences of PONV if none of one or all four of these risk factors are present. In fact, the authors created a risk score with four predictors: female sex, non-smoking status, history of either motion sickness or PONV, and expected use of postoperative opioids (Apfel et al., 1999). Based on available evidence, patients at moderate or high risk of PONV should seek prophylactic antiemetic therapy, and those at high risk should consider combination antiemetic therapy (Elvir-Lazo et al., 2020).

Alternatives or nonpharmacological methods of preventing postoperative nausea and vomiting are being investigated due to the negative effects of classic antiemetics and the high cost of contemporary antiemetics. Consequently, p-6 Acupressure offers a high degree of patient acceptability, is inexpensive, easy to apply, has no side effects, and doesn't interact with drugs, by relasing of endogenous endorphins and the activation of sensory neurons which have antiemetic properties so reducing PONV (Salamah et al., 2023).

In some studies, PONV risks had declined similarly after taking anti-emetic drugs and after P6 acupoint stimulation (Direkvand-Moghadam & Khosravi, 2013).

Although it has become one of the most common surgeries practised nowadays, laparoscopic surgery leads to postoperative nausea and vomiting in the range of 40-80%. Females are at a higher risk of developing this complication due to their gender and the fluctuating of hormones during the menstrual cycle (Maharjan & Bing, 2021) due to follicle-stimulating hormone and estrogen release so PONV may be attached to the pre-ovulatory phase (Hambridge, 2013). Other potential risk factors are exposure to opioids, type of surgical procedure, history of previous PONV, carbon dioxide retention, prolonged surgery, and peritoneal distension due to pneumoperitoneum (Som et al., 2016). However, the exact cause of PONV following laparoscopic surgery with general anaesthesia is unknown. It is most likely multifactorial (Kathuria et al., 2020).

For the purpose of this study, the efficacy of prophylactic metoclopramide as monotherapy and in Combination with P-6 Acupressure stimulation for preventing PONV will be assessed.

1.6 Aim of study

Indeed, the exact aetiology of PONV after laparoscopic surgery with general anaesthesia is unknown. It is most likely multifactorial. This study aims to assess the efficacy of prophylactic metoclopramide as monotherapy and in combination with P-6 Acupressure stimulation for preventing PONV undergoing laparoscopic cholecystectomy surgeries under general anaesthesia.

1.6.1 Objectives of the Study

1. To determine the incidence of PONV in relation to demographic variables.
2. To assess the effect of the administration of metoclopramide on PONV as a single agent.
3. To assess the effect of administration of P-6 Acupressure stimulation on PONV as a single agent.
4. To assess the effect of administration of a Combination of metoclopramide and P-6 Acupressure stimulation on PONV.

1.6.2 Study Hypothesis

H0: There is no significant effect of p-6 Acupressure in reducing PONV after laparoscopic cholecystectomy at a level of 0.05.

H0: There is no significant effect of metoclopramide in reducing PONV after laparoscopic cholecystectomy at a level of 0.05.

H0: There is no significant effect of the Combination of p- 6 Acupressure and metoclopramide in reducing PONV after laparoscopic cholecystectomy at a level of 0.05.

H0: There's no significant difference at the level of 0.05 related to the incidence of PONV between the Combination group (p-6 Acupressure and metoclopramide) and p-6 Acupressure group

H0: There's no significant difference at a level of 0.05 related to the incidence of PONV between the Combination group (p-6 Acupressure and metoclopramide) and metoclopramide group

The first primary endpoint after the conclusion of this study will be the complete response up to 24 hours after surgery. This was defined as no episodes of nausea vomiting, and no requirement for rescue medication. The secondary endpoints were the incidence of nausea and vomiting, the severity of nausea, the use of rescue antiemetic drugs, the time to first requirement for rescue medication, and adverse effects. The methods to be used to determine these endpoints include interviews and patient reports.

Chapter Two
Methodology

2.1 Study Design

A prospective, randomized, double-blind, placebo-controlled trial was performed to evaluate the effect of metoclopramide alone or in Combination with P-6 Acupressure stimulation for the prevention of postoperative nausea and vomiting. Female subjects underwent laparoscopic cholecystectomy under general anaesthesia. Prior to the induction of anaesthesia, both groups of patients underwent laparoscopic cholecystectomy surgery under general anaesthesia.

2.2 Site and Setting

The study was carried out in the West Bank/Palestine surgery department of the Governmental Hospital (Qalqilia).
Data only collecting from one hospital due to diffecult transferring between the cities as a result of occupation and 7th october war.

2.3 Study Population

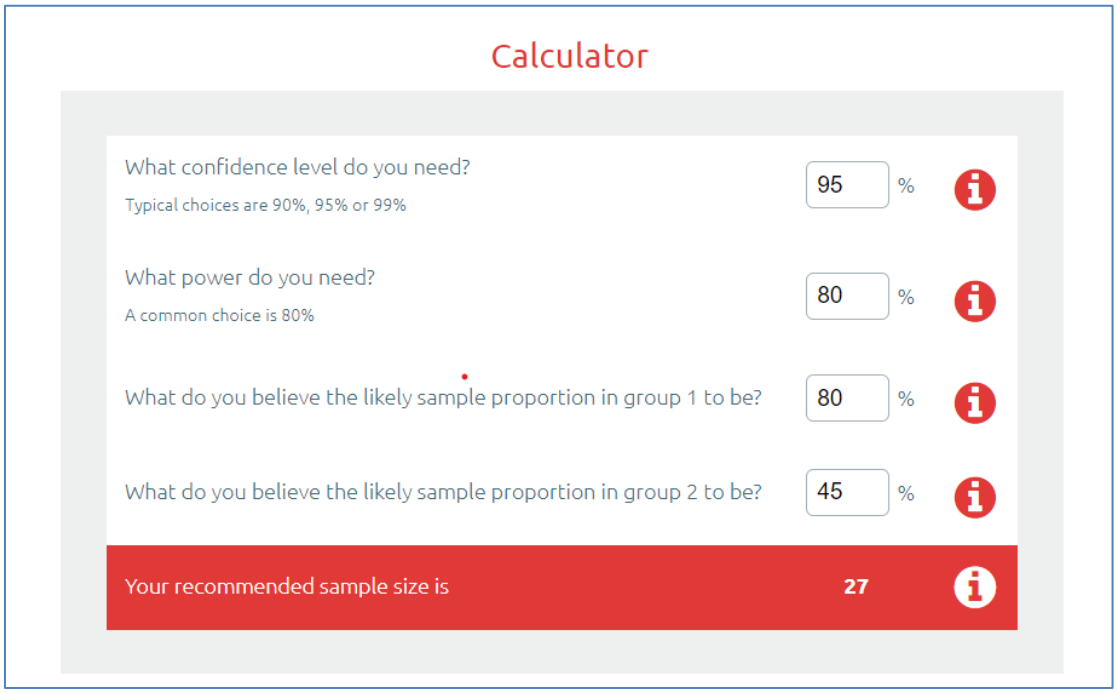
One hundred and twenty females, American Society of Anesthesiologists ASA physical status I and II patients undergoing elective laparoscopic cholecystectomy surgery are randomly assigned to four groups.

2.4 Sample Size and Sampling Method

It was demonstrated that the Acupressure group experienced nausea and vomiting at rates that were significantly lower than those of the control group for the entirety of the postoperative period (16/35 vs 27/33, $p = 0.03$, respectively) with a significance level of 0.05 and power of 90% (Miranda et al., 2020). The sample size was 30 for each group. A total of 120 patients will be taken into the study after adding 10% of the sample for the expected drop-out by using Comparing Two Proportions - Sample Size calculator, if any participant withdrawn from study, data relate to her excluded from study.

Figure 1

Calculator of sample size



2.4.1 Randomization and Blindness

Patients were randomized through the envelope method after taking a consent form to participate. Consequently, a pack of opaque sealed envelopes contains a card with either the words "Group 1, which reflected a Combination of p-6 Acupressure and metoclopramide", "Group 2, which reflected p-6 Acupressure + 1 ml Nacl", "Group 3 which reflected metoclopramide + Placebo Acupressure", or "Group 4 which reflected Placebo Acupressure + 1 ml Nacl" written on it and inserted in the envelope based in coding. Outside the envelope, the number that reflects the type of treatment is written and will be presented to a professional nurse irrelevant to the study. Based on this information, a computerized random generator was used to generate the sequence. As a result, a generator list of 120 numbers is ready now. The envelopes were ordered accordingly based on the generator list number.

Group 1: Combination of p-6 Acupressure and metoclopramide

Group 2: p-6 Acupressure + 1 ml Nacl

Group 3: metoclopramide + Placebo Acupressure

Group 4: Placebo Acupressure + 1 ml Nacl.

2.4.2 Inclusion criteria

- Patients are performed for elective laparoscopic cholecystectomy surgery.
- Female patient.
- Age between 18 to 65 years.
- Weight 45 to 100 kg.
- A risk of = > 40 % for PONV.

A study conducted by Apfel et al. (1999) found that a very simple risk evaluation was made because the factor of being female was reduced to a single issue. Four key predictors were included: female status, a history of motion sickness or postoperative nausea and vomiting, nonsmoking, and the use of opioids after surgery. The PONV rate differed depending on the number of risk factors. With no risk factors, the nominal rate was 10%. The corresponding PONV rates with one, two, three, and four risk factors were 21%, 39%, 61%, and 79%, respectively.

2.4.3 Exclusion Criteria

- History of wrists problem.
- Anatomical or neurological abnormalities of the upper limbs.
- Nausea and vomiting within 24 hours of the operation.
- History of diabetes mellitus.
- Over 100 kg body weight.
- Experience history of utilizing Acupressure.

2.4.4 Dependent Variable

- Rescue antiemetic medication: dexamethasone 8 mg iv.
- Incidence and severity of nausea, frequency of vomiting in post-anesthesia care unit.
- Incidence and severity of nausea and frequency of vomiting in the surgical ward.

2.4.5 Independent Variables

Demographic characteristics: Age, duration of anaesthesia, weight, length of surgery, total dose of perioperative medications, and vital signs: heart rate, temperature, blood pressure, respiratory rate, SpO2, Pramine, P6 acupressure, combination of pramine and P6 acupressure.

2.5 Outcome measurements

The result was tested by using a Likert Scale ranging from (0-6), the measuring severity of PONV. A: 0 indicating no nausea; b: 1 meaning very mild nausea; c: 2; for mild, d: 3; for moderate, e: 4; for severe, f: 5; for very severe, g: 6; for intolerable. So, in general, 3 or more points were considered a requirement of rescue antiemetic administration once.

Secondary outcomes were the adverse effects determined of metoclopramide (headache, fatigue, drowsiness, extrapyramidal symptom) and determined any adverse effect of p-6 Acupressure (mild discomfort, swollen wrists, redness, skin breakdown near wristband, and itching).

2.6 Administration of Treatments Preoperative

2.6.1 Timing of intervention

P6- Acupressure 30 min before anaesthesia induction.

Metoclopramide just before anaesthesia is induced.

2.6.2 Blindness

Neither the participants nor the experimenters knew which treatment they were receiving due to the nurse unrelated to study after training her put the band (for more sure accuret place I put two point if placebo aupressure or acupressure), then cover it with bandages and prepare the medication depend on which group, then participant transfer to operation room, so anesthesiologist and surgon don't know which medication prepare, and give it.

For follow up any time participant want to remove it she call the nurse not relate to study to remove it and re put it after two hour.

2.6.3 Intervention

Group 1: Combination of the P-6 Sea Band acupressure, an acupressure wristband manufactured by Sea Band Ltd. in Leicestershire, UK, has a pressure stud, a tiny 7mm button that resembles a pea in size that is positioned on both wrists thirty minutes before anaesthesia induction and can remain effective for up to 24 hours. To apply it, three fingers breadth using the patient's fingers is recommended approximately five centimetres above the flexor palmar crease. Expressively, metoclopramide 10 mg =1 ml

was administered immediately before anaesthesia induction. Then, the button is inserted about one centimeter-deep between the palmaris longus and flexor carpi radialis tendon.

Group 2: The P-6 Sea Band acupressure, an acupressure wristband manufactured by Sea Band Ltd. in Leicestershire, UK, has a pressure stud, a tiny 7mm button that resembles a pea in size that is positioned on both wrists thirty minutes before anaesthesia induction and can remain effective for up to 24 hours. To apply it, three fingers breadth using the patient's fingers is recommended approximately five centimetres above the flexor palmar crease. The button is inserted about one centimeter-deep between the palmaris longus and flexor carpi radialis tendons. Additionally, 1 millilitre of normal saline solution (0.9%) is administered just before the onset of anaesthesia.

Group 3: Placebo acupressure wrist bands apply pressure to a specific point on the back of the forearm using the patient's fingers positioned near the palm crease for stimulation. The Seabands are positioned on both wrists thirty minutes before anaesthesia and remain in place for up to 24 hours. + Metoclopramide 10 mg =1 ml administered just before induction of anaesthesia.

Group 4: Placebo acupressure wrist bands apply pressure to a specific point on the back of the forearm using the patient's fingers positioned near the palm crease for stimulation. The Seabands are positioned on both wrists thirty minutes before anaesthesia and remain in place for up to 24 hours, and normal saline 0.9% =1 ml is administered just before induction of anaesthesia.

2.6.4 Anesthesia Protocol

Fifteen minutes prior to the anaesthesia being given, the participants received a dose of Dormicum 1 mg through an IV. All participants were given Lactated Ringer's solution at a rate of ten ml per kilogram.

Anesthesia monitoring uses noninvasive blood pressure measurement, electrocardiogram, capnography, and pulse oximetry.

All participants underwent the same anaesthetic technique for consistency. General anaesthesia was initiated using 2 μg/kg of Fentanyl and 2 mg/kg of Propofol along with

0.5 mg/kg of atracurium to facilitate tracheal intubation based on the formula (age/4) +3. Once inserted, the cuff was inflated. The anaesthesia regimen included 1.2% isoflurane and 50% oxygen in oxygen, with ventilation mechanically adjusted and regulated to keep the end-tidal carbon dioxide concentration between 35 and 40 mmHg.

Once the procedure was completed, Atropine was given at a dosage of 0.01 mg/kg, and to undo the muscular relaxation, 0.05 mg/kg of Neostigmine was injected intravenously. After that, the endotracheal tube was taken out. Every single patient was given one gram of paracetamol intravenous after anaesthetic induction. The first dose would be continued every 6 hours postoperatively for the first 24 hours.

The assigned medications were created by an anaesthetist who was unrelated to patient care. All drugs and normal saline were given in the 2 ml syringe containing one ml of either metoclopramide or normal saline similar to each other for the purpose of blindness. Therefore, the drugs were given by the anaesthetist who was responsible for the patient intraoperatively when the operation was finished, and he did not know what each syringe contained.

2.6.5 Surgical Protocol

Patients were placed in reverse Trendelenburg, and the abdomen was inflated with carbon dioxide to bring the intra-abdominal pressure to the level of 13 15 mm Hg. The nasogastric tube was changed to a temporary one, and the tube was put through the nose orally to facilitate drainage. The initial nasogastric tube was again suctioned out and removed from the nasal canal before the breathing tube was removed.

2.6.6 Study procedure

The patient was briefed about the study before it was conducted and was requested to provide consent through a signature. A score was assessed based on the patient's medical history, and examination found him to be at high risk of developing PONV. Patients with a PONV risk over 40%, according to the Apfel Risk Score (Apfel et al., 1999), were invited to participate in the study. They were then randomly assigned to one of four groups within the surgical ward. For all participants, sea bands were applied to both wrists 30 minutes before anaesthesia was administered by a nurse unconnected with the conduct of anaesthesia and postoperative care. After extubation of the trachea, the patients were

transported to the post anaesthetic care unit, where their vital signs were monitored at 15-minute intervals by an observer unconnected with the conduct of the study. During their stay in the PACU, the patient's oxygen saturation was continuously monitored.

Upon arrival in the room, oxygen was provided via a face mask at the rate of 5 litres per minute until the patient was ready to be transferred to the surgical ward. Patients were transferred to the ward for further monitoring. Each patient also received 1 gram of IV paracetamol in the PACU. They were instructed to keep the wrist bands on continuously for a duration of 24 hours. The patient was allowed to remove them at night while sleeping and reapply them in the morning. The bands could be removed if they were uncomfortable every two hours for thirty minutes. The patient brought an assessment form to the surgical ward, which was afterwards given back to the medical personnel along with the Sea Bands.

The control group was monitored similarly to the three groups receiving treatment. After leaving the PACU, they were provided with evaluation forms for their recovery.

Adverse effects of metoclopramide, such as headache, drowsiness, fatigue, blurred vision, constipation or diarrhoea, and extrapyramidal symptoms, were documented.

Adverse effects of the Acupressure band: mild discomfort, swollen wrists, redness, skin breakdown near the wristband, and itching were documented.

2.6.7 Assessment of nausea and Vomiting in the Postoperative Anesthetic Care Unit (PACU)

A Likert scale score that goes from 0 to 6 indicates the level of nausea as follows 0 represents no nausea, 1 stands for very mild nausea, 2 indicates mild nausea, 3 signifies moderate nausea, 4 denotes severe nausea, 5 corresponds to very severe nausea and 6 indicates intolerable nausea leading to vomiting.
Three scores and above are defined as nausea requiring a single administration of an antiemetic drug.

- The patients will be requested to measure their level of nausea upon arrival and then every hour until they are discharge from the PACU.
- The nurses will note vomiting, as well as the requirement for antiemetic if the patient

vomits twice or more.

- Retching was classified together with vomiting.

2.6.8 Assessment of nausea and vomiting after discharge from PACU

Nausea and vomiting were noted during a period post-discharge from the PACU on the day of surgery and up to 24 hours later, for which the study was terminated at this point.

2.6.9 Rescue antiemetic medication

If the nausea is more than ≥ 3 on the Likert scale and/or vomiting twice and above. Decort® (dexamethasone 8 mg IV).

2.6.10 Assessment of patient satisfaction

patients assessed how satisfied they were with the treatment they received for nausea and vomiting using a Lickert-type scale of 0-6, in which 0 = very much dissatisfied and 6 = very much satisfied.

2.7 Ethical consideration

The study done in this thesis was in line with the Helsinki Declaration. The Ministry of Health has consented, and An-Najah National University's Institutional Research Board has legally approved the research. Treatment randomization is an ethical issue since it contravenes the fact that a patient should be able to consent to the treatment.

Before deciding whether to take part in the study, every single patient received information, both written and verbal, regarding the purpose and goals of the research. It was explicitly stated that joining the study was optional and could be withdrawn at any moment, and confidentiality would be upheld. As a result, the ethical dilemma was considered to be minimal.

Nevertheless, irrespective of the group they were randomly assigned to, every patient got prophylactic treatment to avoid PONV and rescue medication when necessary. The consent form highlights the anonymity of data collection. It clearly states that the data will solely be used for research purposes, and participants can choose to withdraw from the study whenever they want.

2.8 Informed Consent

The researcher was provided with both written and spoken details regarding the research and was given the chance to seek clarification. The researcher understood that joining this study is optional and that participants have the right to withdraw at any point without providing any reason.

2.9 Validity and Reliability

Several studies confirmed that the Likert scale (0-6) had an excellent test-retest reliability (Agarwal et al., 2002).

To ensure the reliability of this research, Cronbach Alpha was computed using the Statistical Package for Social Sciences SPSS with a threshold value set at 0.78 (78%) as an acceptable benchmark.

2.10 Data Analysis Plan

The data analysis process was done using SPSS Version 23. Only the patients who took part in and completed the study were included in the results. Descriptive statistics used included standard deviation, mean, frequency, and percentage. The Chi-square test was implemented to examine proportions among more than two groups, while one-way ANOVA was applied to compare means between two distinct groups. A significance level of $p < 0.05$ was applied to statistical data.

Chapter Three

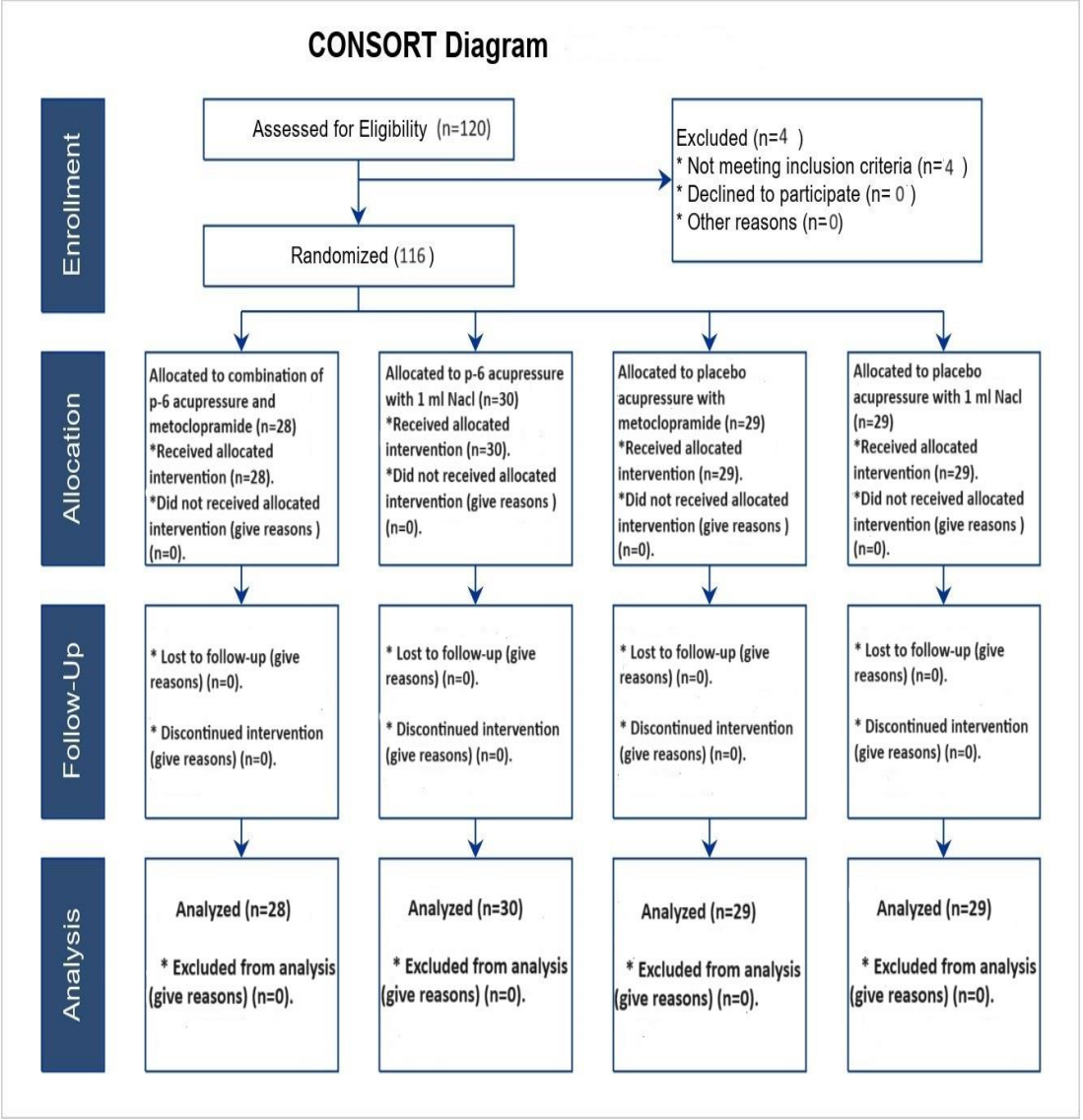
Results

3.1 Introduction

One hundred and twenty patients were assigned for eligibility, but only one hundred and sixteen female patients were randomly allocated to the Combination group (n= 28), Acupressure group (n= 30), metoclopramide group (n= 29), and Placebo group (n=29).

Figure 2

CONSORT Flow Diagram of female patient enrollment and assignment to the four groups



3.2 Patient Characteristics and Demographic Data

There are no significant differences at 0.05 level between the study groups (Combination, Acupressure, Pramin, Placebo) in all the demographic data and patient characteristics, whereas all the P-values are higher than 0.05 levels, as shown in Table (1).

Table 1

Patient Characteristics and Demographic Data

Variable	Group				P-value
	Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	
Age	41.5 ± 7.36	43.7 ± 8.45	42.55 ± 7.51	42.93 ± 8.27	0.764
History of PONV	7(25%)	7(23.3%)	7(24.1%)	6(20.7%)	0.983
History of motion sickness	23(82.1%)	24(80%)	24(82.8%)	23(79.3%)	0.984
Planning for opioid	28(100%)	30(100%)	29(100%)	29(100%)	-----
Smoking	17(60.7%)	15(50%)	15(51.7%)	15(51.7%)	0.848
Apfel risk score:					
10%	0(0%)	0(0%)	0(0%)	0(0%)	
>= 20%	0(0%)	0(0%)	0(0%)	0(0%)	0.978
>= 40%	1(3.6%)	1(3.3%)	1(3.4%)	1(3.4%)	
>= 60%	20(71.4%)	19(63.3%)	18(62.1%)	17(58.6%)	
>= 80%	7(25%)	10(33.3%)	10(34.5%)	11(37.9%)	
Weight	73.82 ± 9.08	72.7 ± 9.67	73.76 ± 9.48	73.62 ± 8.18	0.961
Height	159.71 ± 2.55	161.4 ± 4.9	159.86 ± 3.72	161.28 ± 3.76	0.197
BMI	28.95 ± 3.64	28.26 ± 4.22	28.91 ± 4.01	28.29 ± 3	0.828

Note: Significant at 0.05, Frequencies, and Percentages (%), Data are Mean ±SD with P-values derived from one-way ANOVA.

3.3 Data collection in the operating room, PACU, ward, and during the first 24 hours following surgery

The results in Table (2) show that there are significant differences at 0.05 level between the study groups (Combination, Acupressure, Pramin, Placebo) only in the Total propofol, End-tidal isoflurane concentration, and in the End-tidal Co2.

Table 2

Data collection in the operating room, PACU, Ward, and during the first 24 hours following surgery

Variable	Group				P-value
	Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	
Total fentanyl	200 ± 0	200 ± 0	200 ± 0	200 ± 0	-----
Total propofol\ mg	197.86 ± 8.33	211.67 ± 28.78	201.38 ± 15.75	198.62 ± 10.6	0.013
End-tidal isoflurane concentration	1.5 ± 0.38	1.92 ± 0.49	1.71 ± 0.41	1.52 ± 0.37	0.000
End-tidal Co2, mmHg	42.64 ± 4.65	37.83 ± 5.55	41.21 ± 5.46	42.93 ± 3.88	0.000
Duration of surgery	54.11 ± 7.46	53 ± 7.61	54.31 ± 7.41	53.28 ± 7.59	0.891
Duration of anaesthesia (min)	69.11 ± 7.46	67.5 ± 8.59	69.31 ± 7.41	68.1 ± 7.49	0.787
Intraoperative fluid intake	1014.29 ± 52.45	1040 ± 81.37	1020.69 ± 61.99	1013.79 ± 51.58	0.347
Intraoperative Fio2	100 ± 0	100 ± 0	100 ± 0	100 ± 0	-----

Note: Significant at 0.05, Frequencies, and Percentages (%), Data are Mean ±SD with P-values derived from one-way ANOVA.

For the total propofol, the post-hoc pairwise mean comparisons test result showed that the acupressure group's mean was significantly higher than that of the combination group and higher than the placebo group's mean with P = 0.013. The Mean of the Acupressure group = was 211.67, the Combination group = 197.86 and the Placebo was 198.62.

Regarding the Total End-tidal isoflurane concentration, the results of the post-hoc pairwise mean comparisons test showed that the mean of the Acupressure group (Mean=1.92) is only significantly higher than the mean of the Combination group (Mean=1.5) and also higher than the mean of the Placebo group (Mean=1.52), the P-value of the test is 0.000.

Finally, regarding the End-tidal CO2, post-hoc pairwise mean comparisons result shown below that the mean of the Acupressure group (Mean=37.83) is significantly less than all the mean values of the other groups: Combination group (Mean=42.64) than the Placebo group (Mean=42.93), and Pramin group (Mean=41.21), the P-value of the test is 0.000.

Table 3

Mean comparisons for significant Intraoperative Information in PACU

Dependent Variable	Group (I)	Group (J)	Mean Difference (I-J)	P-value
Total propofol	Combination	Acupressure	-13.810	0.021
		Pramin	-3.522	0.880
		Placebo	-0.764	0.999
	Acupressure	Combination	13.810	0.021
		Pramin	10.287	0.128
		Placebo	13.046	0.031
	Pramin	Combination	3.522	0.880
		Acupressure	-10.287	0.128
		Placebo	2.759	0.936
	Placebo	Combination	0.764	0.999
		Acupressure	-13.046	0.031
		Pramin	-2.759	0.936
End-tidal isoflurane concentration	Combination	Acupressure	-.4167	0.001
		Pramin	-0.2069	0.247
		Placebo	-0.0172	0.999
	Acupressure	Combination	.4167	0.001
		Pramin	0.2098	0.222
		Placebo	.3994	0.002
	Pramin	Combination	0.2069	0.247
		Acupressure	-0.2098	0.222
		Placebo	0.1897	0.314
	Placebo	Combination	0.0172	0.999
		Acupressure	-.3994	0.002
		Pramin	-0.1897	0.314
End-tidal Co2	Combination	Acupressure	4.810	0.002
		Pramin	1.436	0.692
		Placebo	-0.288	0.996
	Acupressure	Combination	-4.810	0.002
		Pramin	-3.374	0.048
		Placebo	-5.098	0.001
	Pramin	Combination	-1.436	0.692
		Acupressure	3.374	0.048
		Placebo	-1.724	0.547
	Placebo	Combination	0.288	0.996
		Acupressure	5.098	0.001
		Pramin	1.724	0.547

Note: Significant at 0.05, Post-hoc pairwise mean comparisons test adjusted using the Tukey correction.

3.4 Vital Signs in Total 24 Hours

There are only a statically significant differences at 0.05 level between the study groups (Combination, Acupressure, Pramin, Placebo) only in the SBP, DBP, and MAP, as shown in Table (4).

Table 4

Vital Signs in Total 24 hours between Study Groups

Variable	Group				P-value
	Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	
Total SBP	112.19 ± 5.8	116.82 ± 5.54	115.64 ± 5.17	110.33 ± 2.75	0.000
Total DBP	66.06 ± 3.97	68.82 ± 5.61	69.25 ± 4.49	64.66 ± 3.21	0.000
Total MAP	81.67 ± 3.74	85.05 ± 5.49	84.62 ± 3.99	80.04 ± 2.78	0.000
Total RR	16.1 ± 1.36	16.04 ± 1.34	15.71 ± 0.91	15.66 ± 1.06	0.381
Total SPO2	98.12 ± 1.13	97.68 ± 2.05	98.14 ± 1.03	98.35 ± 0.93	0.290
Total Pulse	82.59 ± 5.82	81.45 ± 6.13	84.42 ± 6.74	83.08 ± 5.17	0.298

Note: Significant at 0.05, Frequencies, and Percentages (%), Data are Mean ±SD with P-values derived from one-way ANOVA.

For the total propofol, the post-hoc pairwise mean comparisons test result showed that the acupressure group's mean was significantly higher than that of the combination group and higher than the placebo group's mean with P = 0.013. The Mean of the Acupressure group = was 211.67, the Combination group = 197.86 and the Placebo was 198.62.

Regarding the DBP, the Acupressure group (Mean=68.82) is only significantly higher than the Placebo group (Mean=64.66), while the Pramin group (Mean=69.25) is significantly higher than the Combination group (Mean=66.06) and also higher than the Placebo group (Mean=64.66), the P-value of the test is 0.000 as shown in table (4, 5).

Finally, regarding the MAP, the Acupressure group (Mean=85.05) and the Pramin group (Mean=84.62) are significantly higher than the Combination group (Mean=81.67) and also higher than the Placebo group (Mean=80.04), the P-value of the test is 0.000 as shown in table (4, 5).

Table 5

Mean comparisons for significant Vital Signs in the total 24 hours between Study Groups

Dependent Variable	Group (I)	Group (J)	Mean Difference (I-J)	P-value
Total SBP	Combination	Acupressure	-4.629	0.003
		Pramin	-3.452	0.048
		Placebo	1.859	0.493
	Acupressure	Combination	4.629	0.003
		Pramin	1.177	0.799
		Placebo	6.489	0.000
	Pramin	Combination	3.452	0.048
		Acupressure	-1.177	0.799
		Placebo	5.311	0.000
	Placebo	Combination	-1.859	0.493
		Acupressure	-6.489	0.000
		Pramin	-5.311	0.000
Total DBP	Combination	Acupressure	-2.763	0.088
		Pramin	-3.195	0.037
		Placebo	1.397	0.634
	Acupressure	Combination	2.763	0.088
		Pramin	-0.431	0.982
		Placebo	4.160	0.003
	Pramin	Combination	3.195	0.037
		Acupressure	0.431	0.982
		Placebo	4.591	0.001
	Placebo	Combination	-1.397	0.634
		Acupressure	-4.160	0.003
		Pramin	-4.591	0.001
Total MAP	Combination	Acupressure	-3.378	0.013
		Pramin	-2.949	0.040
		Placebo	1.632	0.447
	Acupressure	Combination	3.378	0.013
		Pramin	0.429	0.979
		Placebo	5.010	0.000
	Pramin	Combination	2.949	0.040
		Acupressure	-0.429	0.979
		Placebo	4.581	0.000
	Placebo	Combination	-1.632	0.447
		Acupressure	-5.010	0.000
		Pramin	-4.581	0.000

Note: Significant at 0.05, Post-hoc pairwise mean comparisons were adjusted using the Tukey correction

Figure 3

Mean of SPB, DPB, MAP in Total 24 hours for female patients undergoing laparoscopic cholecystectomy between study groups

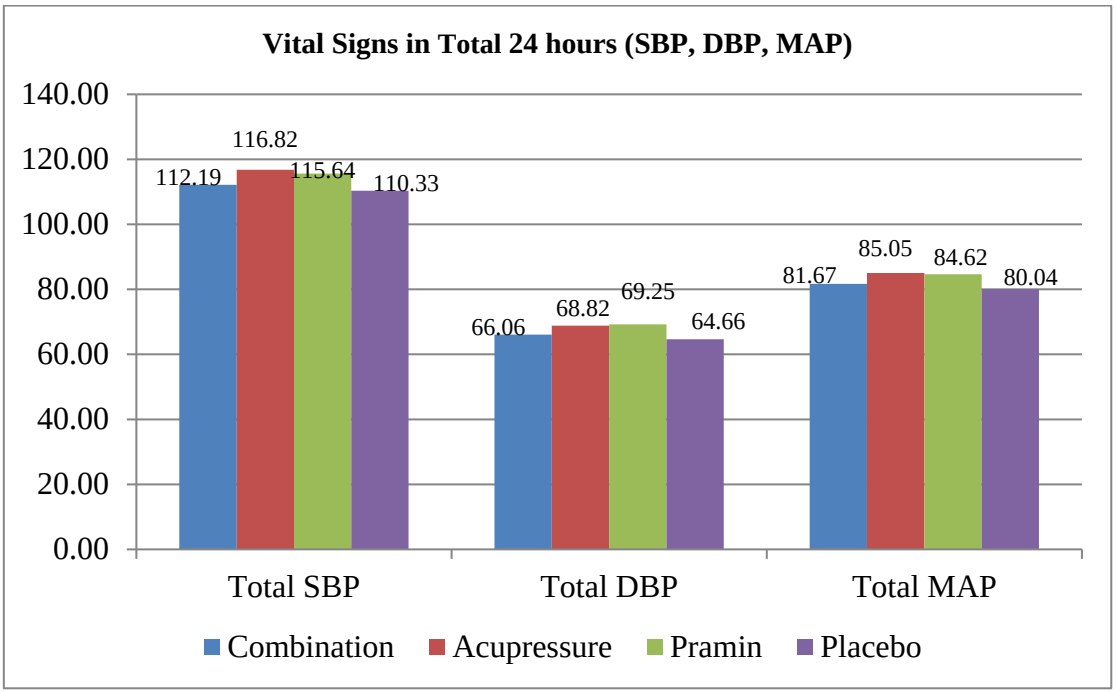
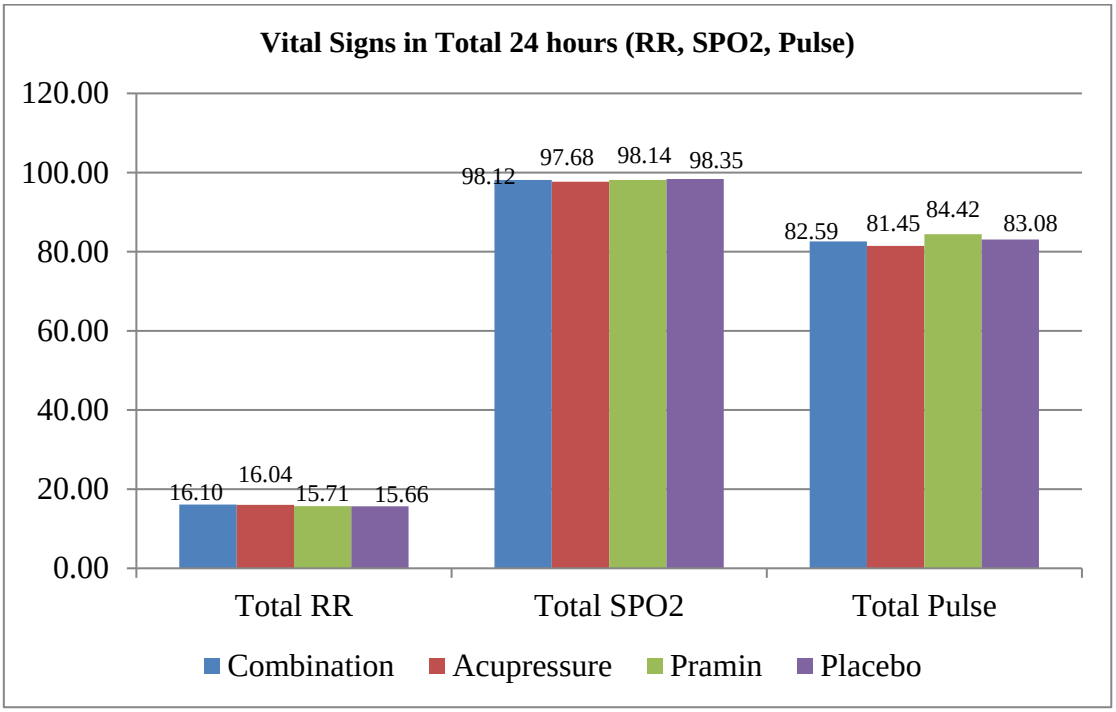


Figure 4

Mean of RR, SPO2, and Pulse in Total 24 hours for female patients undergoing laparoscopic cholecystectomy between study groups.



3.5 The Incidence of Postoperative Nausea, Vomiting, Intensity of Nausea in PACU, Ward and in Total 24 hours

We show the results of Table 6, which show that ($p < 0.05$). This is evidence of the existence of significant statistical differences between the study groups in the occurrence of nausea in the postoperative care unit, in the ward, and in total for 24 hours.

Table 6

The incidence of postoperative nausea, vomiting, and the intensity of nausea in PACU, ward, and in total 24 hours between study groups

Variable	Group Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	P-value
Incidence of nausea (In PACU)	1(3.6%)	8(26.7%)	10(34.5%)	18(62.1%)	0.000
Incidence of nausea (In Ward)	4(14.3%)	5(16.7%)	10(34.5%)	14(48.3%)	0.012
Incidence of nausea (In Total 24 hrs.)	5(17.9%)	8(26.7%)	10(34.5%)	18(62.1%)	0.003
Intensity of nausea (In PACU)	0.14 ± 0.76	0.93 ± 1.78	1.41 ± 2.08	2.21 ± 1.99	0.000
Intensity of nausea (In Ward)	0.18 ± 0.46	0.27 ± 0.62	0.32 ± 0.5	0.47 ± 0.65	0.276
Intensity of nausea (In Total 24 hrs.)	0.17 ± 0.39	0.4 ± 0.77	0.54 ± 0.77	0.81 ± 0.86	0.011
Incidence of vomiting (In PACU)	1(3.6%)	4(13.3%)	8(27.6%)	14(48.3%)	0.000
Incidence of vomiting (In Ward)	3(10.7%)	3(10%)	4(13.8%)	10(34.5%)	0.042
Incidence of vomiting (In Total 24 hrs.)	4(14.3%)	6(20%)	11(37.9%)	17(58.6%)	0.001

Note: Significant at 0.05, Data are Mean ±SD with P-values derived from one-way ANOVA, Frequencies, and Percentages (%) with P-values derived from the Chi-Square test.

3.6 Incidence of Vomiting

Regarding vomiting in PACU, there is a significant difference in the study groups Combination group 1(3.6%), Acupressure group 4(13.3%), Pramin group 8(27.6%), and Placebo group 14(48.3%) with p-value (0.000). To know where exactly the difference exists, the Post Hoc test was performed, and the result showed a statistically significant difference between the Combination and Pramin groups. There was a significant difference between the Combination and Placebo groups. There were also significant differences between Acupressure and Placebo group p-value < 0.05. However, there is an insignificant difference between the Combination and Acupressure groups, the Acupressure and Pramin groups, and the Pramin and Placebo groups. Thus, vomiting

could be reduced using an Acupressure or a Combination group. Nonetheless, the Combination effect stood out as clearly more effective than the other groups, as shown in Tables (6 and 7).

When comparing Combination group 3(10.7%) and Acupressure group 3(10%) to Placebo group 10(34.5%) on the ward, the proportion of patients reporting vomiting dropped significantly (p-value: 0.042). Pramin group 4(13.8%) and Placebo group 10(34.5%) do not differ significantly from one another. Therefore, compared to the placebo and medication group, the results show that acupressure alone or in combination is more effective at reducing the occurrence of vomiting, as shown in Table (6, 7).

Post hoc test was used to determine the exact location of the statistical difference, and there was a significant difference between the study groups, vehicle group 4 (14.3%), pressure group 6 (20%), bramin group 11 (37.9%) and placebo group 17 (58.6%) with p-value 0.001. The results showed a statistically significant difference between Combination and Pramin and combination and Placebo groups. In addition, there was a significant difference between the Acupressure group and Placebo with a p-value < 0.05. There are insignificant differences between the Combination group and the Acupressure group, between the Acupressure group and the Pramin group, or between the Pramin group and the Placebo group, so the Acupressure group or Combination group could reduce vomiting. Nevertheless, the Combination effect was distinctly more impressive than the other groups, as shown in Tables (6 and 7).

Table 7

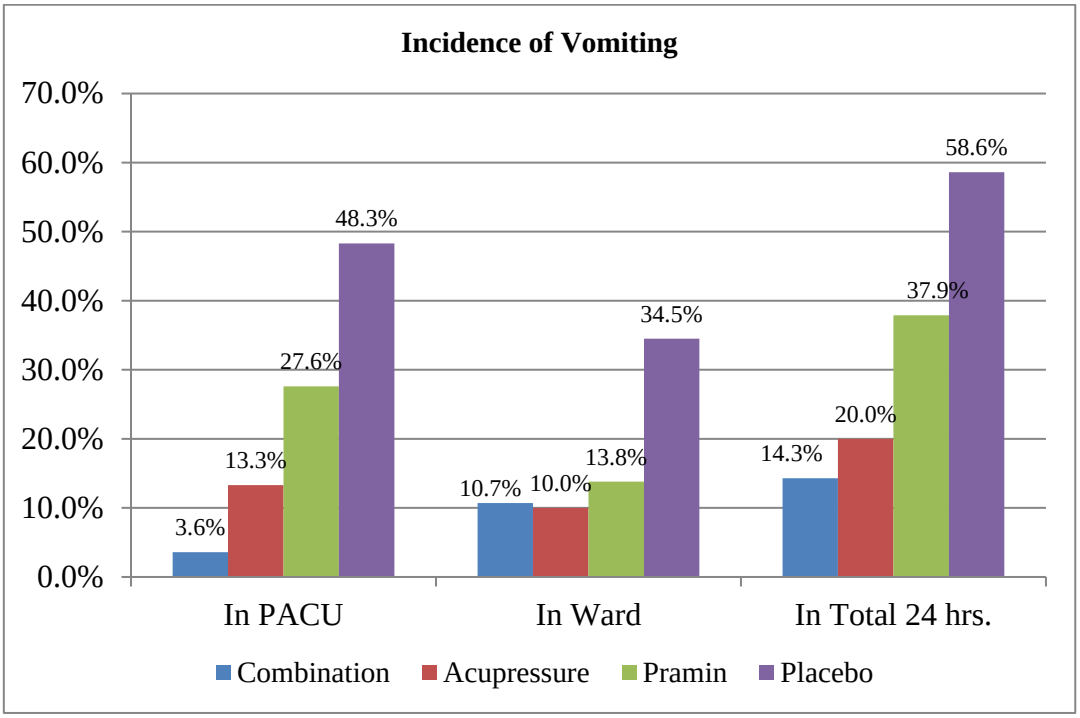
Frequencies comparison for significant postoperative nausea and vomiting between study groups

Variable	Group			
	Combination (A)	Acupressure (B)	Pramin (C)	Placebo (D)
Incidence of nausea (In PACU)	----	----	A	A B
Incidence of nausea (In Ward)	----	----	----	A B
Incidence of nausea (In Total 24 hrs.)	----	----	----	A B
Incidence of vomiting (In PACU)	----	----	A	A B
Incidence of vomiting (In Ward)	----	----	----	A B
Incidence of vomiting (In Total 24 hrs.)	----	----	A	A B

Note: Significant at 0.05, Post-hoc pairwise mean comparisons were adjusted using the Bonferroni correction.

Figure 5

Incidence of vomiting by percentage in PACU, Ward and during a total of 24 hours



3.7 Incidence of Nausea

The study groups Combination group 1 (3.6%), Acupressure group 8 (26.7%), Pramin group 10 (34.5%), and Placebo group 18 (62.1%) differ significantly from one another with p value 0.000. A Post Hoc test was employed to determine the precise location of the statistical difference. The Combination and Phramin groups were statistically significantly different from each other. Further, the difference between the Acupressure and Placebo groups was considered insignificant compared to the Combination groups since the p-value was less than 0.05. As for others, there were insignificant differences between the Combination group and the Acupressure group, between the Acupressure group and the Pramin group, and between the Phramin group and the Placebo group. Therefore, it is possible to state that nausea can be reduced by either an Acupressure group or a Combination group. Nevertheless, the Combination effect was distinctly more impressive than the other groups, as shown in Tables (6 and 7).

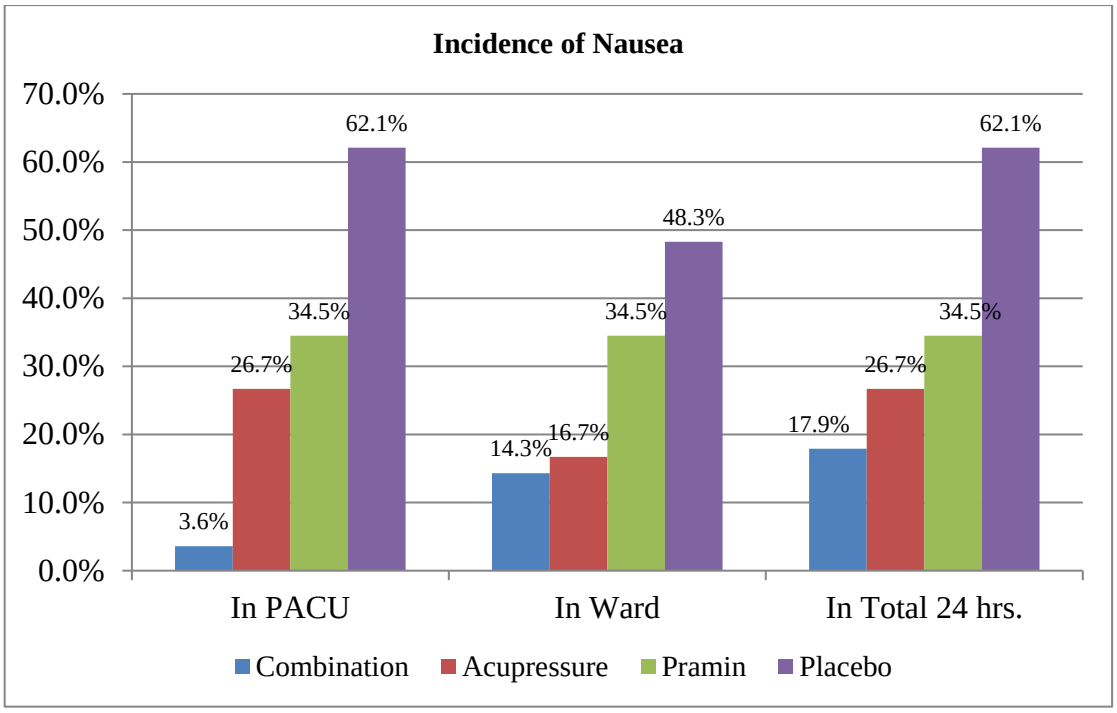
Comparison of the proportion of Patients having nausea among Placebo group 14 and Combination group 4 with a p-value of 0.012 is significant. The number of patients having nausea should decrease in the ward between Combination Group 4 at 14.3% and

Acupressure Group 5 at 16.7% compared to Placebo Group 14 at 48.3%. There is no difference between Pramin group 10, 34.5%, and Placebo group 14, 48.3%. It is understood from the results that the effectiveness of acupressure in reducing nausea is higher whether taken either alone or in combination with Pramin and the placebo group, as shown in Tables (6 and 7).

In a total of 24 hours, there was a significant difference between the treatment groups Combination 5(17.9%) and Acupressure 8(26.7%) compared to Placebo group 18(62.1%) with p-value < 0.05. There are no significant differences between Pramin 10(34.5%) and other study groups; therefore, the result shows that Acupressure, whether administered alone or in combination, is found to be more successful in reducing the frequency of nausea as compared to the Pramin and Placebo group as shown in Tables (6 and 7).

Figure 6

Incidence of nausea by percentage in PACU, Ward, and in the total of 24 hours



3.8 Intensity of Nausea

As it appears from Table 6.8, in PACU, the combination group and acupressure group had significantly less nausea than the Placebo group, and the p-value was less than 0.05. There are statistically significant differences between the Combination group versus the

Pramin group at p=0.034 and the Placebo group at p=0.000, and there are statistically significant differences between the Acupressure group and the Placebo group at p=0.029. There is no significant difference between the Pramin group and Placebo p=0.310. Results show that combination treatment decreased the nausea intensity of patients in PACU compared with acupressure, Pramin, and Placebo. Nevertheless, it was found that combination therapy is superior.

In the ward, table (6) shows that there are no significant differences between the Combination group (0.18), Acupressure group (0.27), Pramin group (0.32), and Placebo group (0.47) with p value of 0.267.

Table 6.8 shows that the summary period is 24 hours. There was a big standard between the combination cure group and the placebo group with a worth of (p 0.006). However, there was a small difference between the mixture therapy team, the stress and anxiety therapy team, and the Bramin group, which had a value associated with p>0.05. Furthermore, there was a tiny difference between the placebo group using the pressure remedy group and the Bramin group, which had an association with p>0.05. Below our analysis, we have research that combination therapy significantly decreases the built-up score of nausea severeness within the 1st day after surgery compared to the placebo group.

Table 8

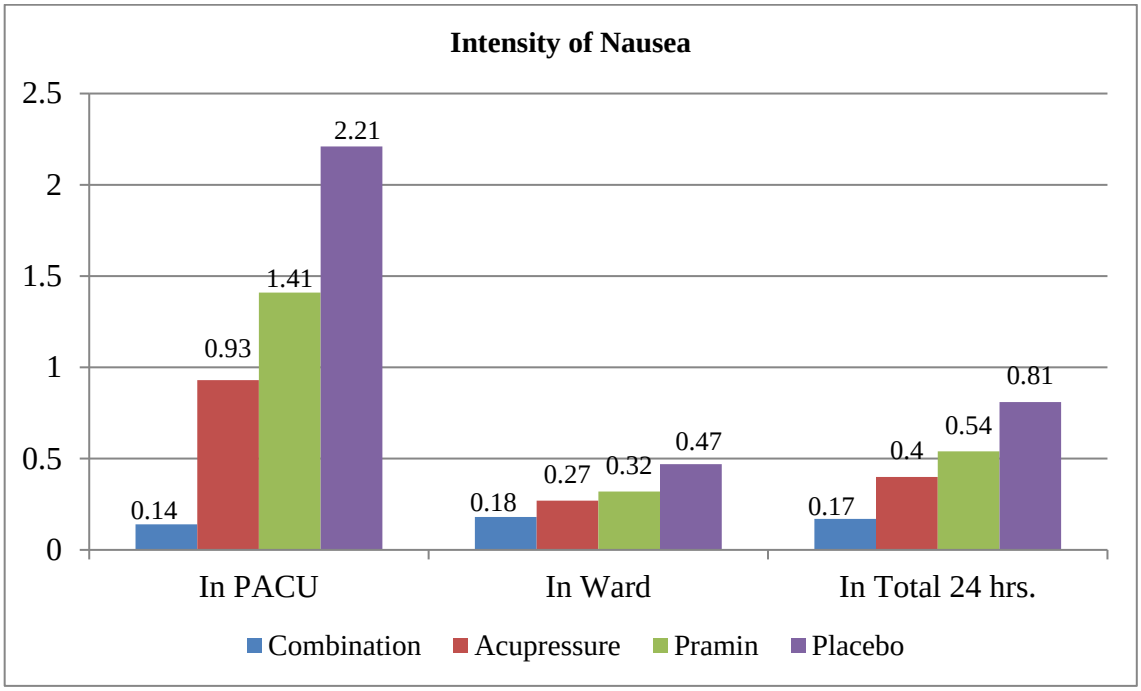
Mean comparisons for the significant intensity of nausea between Study Groups

Dependent Variable	Group (I)	Group (J)	Mean Difference (I-J)	P-value
Intensity of nausea (In PACU)	Combination	Acupressure	-0.790	0.314
		Pramin	-1.271	0.034
		Placebo	-2.064	0.000
	Acupressure	Combination	0.790	0.314
		Pramin	-0.480	0.714
		Placebo	-1.274	0.029
	Pramin	Combination	1.271	0.034
		Acupressure	0.480	0.714
		Placebo	-0.793	0.310
	Placebo	Combination	2.064	0.000
		Acupressure	1.274	0.029
		Pramin	0.793	0.310
Intensity of nausea (In Total 24 hrs.)	Combination	Acupressure	-0.229	0.629
		Pramin	-0.367	0.231
		Placebo	-0.642	0.006
	Acupressure	Combination	0.229	0.629
		Pramin	-0.138	0.885
		Placebo	-0.414	0.132
	Pramin	Combination	0.367	0.231
		Acupressure	0.138	0.885
		Placebo	-0.276	0.472
	Placebo	Combination	0.642	0.006
		Acupressure	0.414	0.132
		Pramin	0.276	0.472

Note: Significant at 0.05, the post-hoc pairwise mean comparisons test was adjusted using the Tukey correction.

Figure 7

Intensity of nausea in PACU, Ward, and during a total of 24 hours



3.8.1 Complete Response

The results in Table (9) show significant differences between the study groups with regard to patients who responded completely (no nausea, no vomiting, and no need for antiemetic medication) with a p-value of 0.003 for the groups (combination therapy, pressure therapy, pramin therapy, placebo).

Table 9

Comparisons between the study groups for the Patients with Complete Response in Total 24 hours

Variable	Group				P-value
	Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	
Complete Response	23(82.1%)	22(73.3%)	18(62.1%)	11(37.9%)	0.003
Incidence of PONV	5(17.9%)	8(26.7%)	11(37.9%)	18(62.1%)	

Note: Significant at 0.05, Frequencies, and Percentages (%), Data are Mean ±SD with P-values derived from one-way ANOVA.

Tables 9 and 10 indicate that there is a significant difference at 0.05, and there is a marked difference in the complete response at a total 24hr by Combination 23[82.1%] and Acupressure 22 [73.3%] versus Placebo 11 [37.9%]. There is no marked difference between the combination group and the acupressure group, the Pramin group, the acupressure group, the Pramin group, the Placebo group, the Pramin group, and the Placebo group. There is no marked difference between the Acupressure and Pramin groups, Placebo groups and Pramin groups, and Placebo groups. Hence, the result shows that the number of patients with complete responses and the acupressure effect are better than other groups.

Table 10

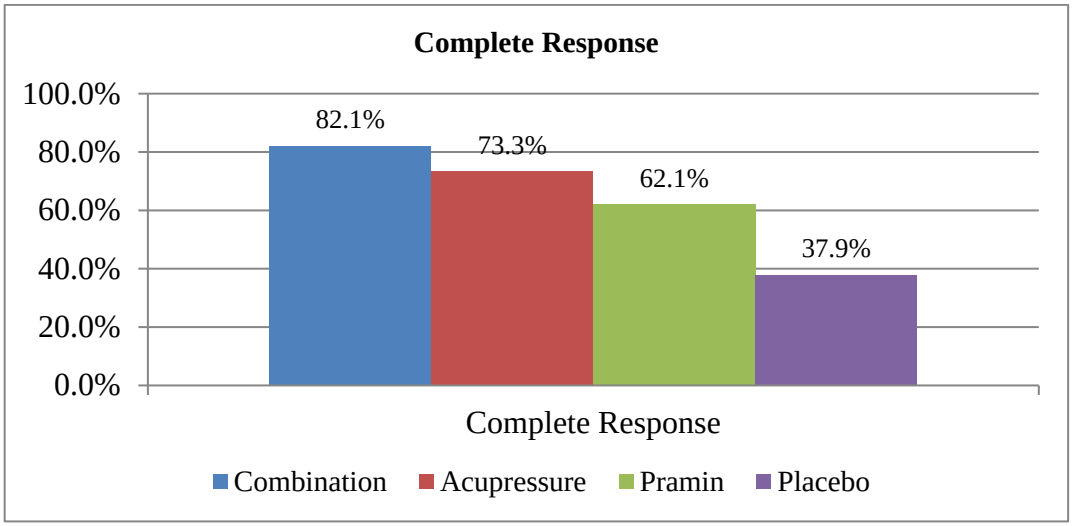
Frequencies comparison for significant complete response between study groups in a Total of 24 hours

Variable	Group			
	Combination (A)	Acupressure (B)	Pramin (C)	Placebo (D)
Complete response	D	D	----	----

Note: Significant at 0.05, Post-hoc pairwise mean comparisons test adjusted using the Bonferroni correction.

Figure 8

Complete Response (no nausea, no retching, no vomiting, and no need for rescue medication) in the four study groups for a total of 24 hr



3.9 Postoperative Symptoms

From the outcomes tabulated in Table 11 in the Appendix, it is clear that there was no significant difference in all of these postoperative symptoms, namely fatigue, headache, drowsiness, Li blurred vision, constipation, diarrhea, and extrapyramidal symptoms. The difference was to be established between groups of patients if the $p < 0.05$.

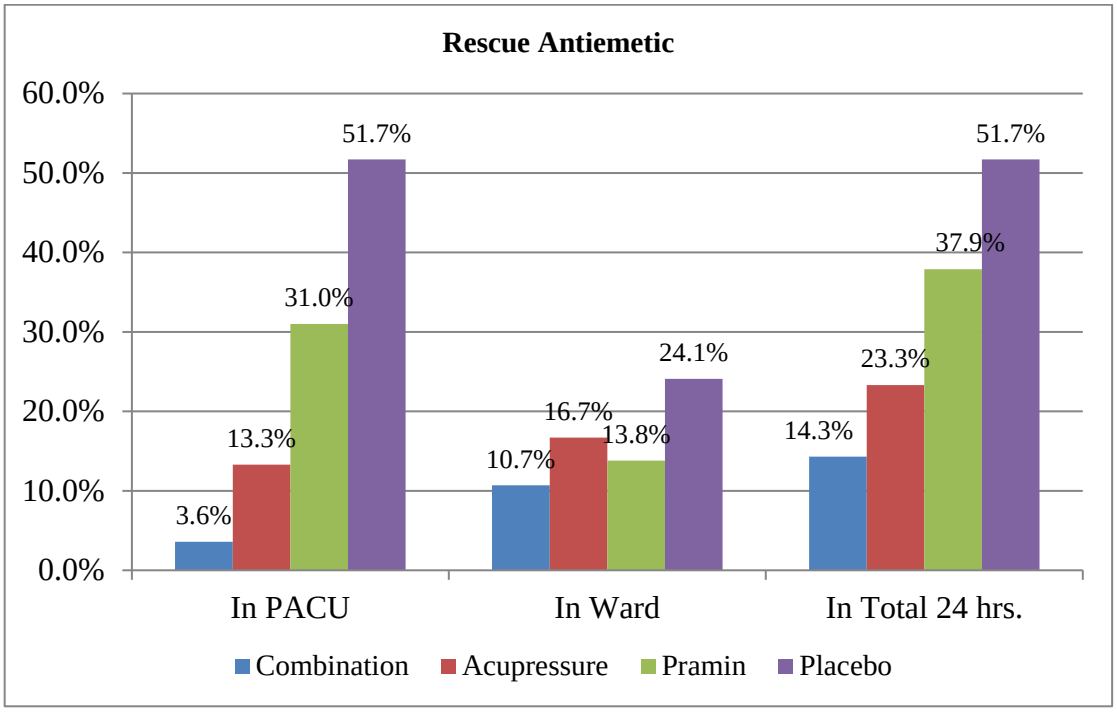
3.10 Rescue Antiemetic (Dexamethasone)

The different proportions indicate the extent of each group's needs in the postoperative care unit. There were no significant differences in the postoperative care unit, in the ward or in the total 24-hour postoperative period, as shown by our p-value > 0.05. The proportions were distributed as follows, as shown in Appendix F of Table 13. The groups were distributed as follows (1 (3.6%) and acupressure 4 (13.3%) to rescue antiemetics significantly less than the placebo group 15 (51.7%) $p < 0.05$. There was no significant difference between group 1 (3.6%) versus group 9 (31%).

The total 24-hour shows that Combination group 4 (14.3%) and Acupressure group 7(23.3%) are significantly less likely to use rescue antiemetics than Placebo group 15(51.7%), $p < 0.05$. However, there are insignificant differences between Pramin group 11(37.9%) and other study groups in the total 24-hour $p>0.05$. The findings indicate that employing Acupressure independently or in Combination decreases the rescue antiemetics requirement within 24 hours postoperatively.

Figure 9

Percentages of patients requiring rescue antiemetic in each period



3.11 Acupressure Side Effects

The results in Table 14 in Appendix (F) show significant differences between the study groups only in Swollen wrists and Itching In the Ward and in Total 24 hours.

Nonetheless, according to Table (14,15) in Appendix (F), there is a significant difference for swollen wrists in Acupressure group 5(16.7%) and Pramin Group 5(16.7%) versus Combination group 0(0) and Placebo group 0(0) with p-value 0.014 in the ward and the total 24 hours. There are no significant differences between the Combination group and the Placebo group, as well as between the Acupressure group and the Pramin group for the number of swollen wrists in the ward or in a total of 24 hours.

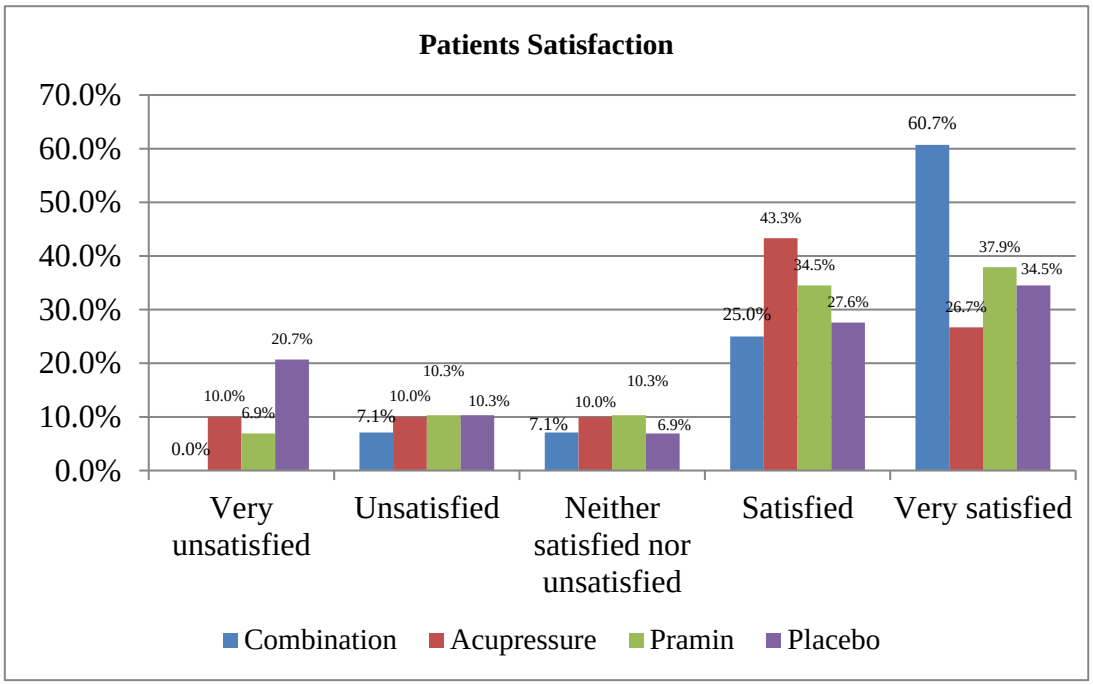
Tables 14 and 15 show the overall satisfaction on the 24-hour self-report. Itching was the only item that showed a significant difference between the placebo group 6 (20.7%) and the combination therapy group 0 (0%), p = 0.041 in all sections. Thus, almost all patients, 24 (85.7%) in the combination therapy group, were satisfied with their health status, while the ratio of satisfied to dissatisfied was 21 (70%) to 6 (20%) in the acupuncture group.

The number of patients who reported dissatisfaction was 5, which is equivalent to 17.2%

in the placebo group. Also, 21 patients, representing 72.4% of the metoclopramide group, expressed satisfaction with their health condition. The number of satisfied patients was found to be 19, representing 31%, compared to 18 (62.1%) in the other group who felt satisfied. It is worth noting that the patients in the acupuncture group and another part of 21 (72.4%) who felt satisfied with their health condition reported high satisfaction, as shown in Figure 9.

Figure 10

Self-report satisfaction rate of patients related to health status in each study group



Chapter Four
Discussion

This study aimed to assess the effectiveness of metoclopramide alone and in combination with P-6 acupressure stimulation for preventing postoperative nausea and vomiting in women undergoing laparoscopic surgery. Past research indicated a 62.1% incidence of PONV among patients who received a placebo after such operations, which have an estimated 75% baseline risk markedly higher than other surgical procedures. The researchers sought to determine if antiemetic therapy could reduce PONV incidence compared to patients who did not receive treatment following laparoscopic procedures (Bameshki et al., 2018). PONV might occur as a result of enhanced intraabdominal pressure that could occur from manipulation of the abdomen and the gastrointestinal tract in the head-down Trendelenburg position; chiefly, insufflation of the abdomen increases pressure on the Vagus nerve that stimulates the centre of the cerebrum where vomiting is initiated (Lingle, 2019; Stoops & Kovac, 2020).

4.1 Risk factors

when deciding whether to use antiemetic drugs as preventive agents for surgeries with a moderate risk of PONV, it is reasonable to consider using them. In addition, in patients with high risks of PONV, it is also logical to consider the use of combination antiemetic treatment (Elvir-Lazo et al., 2020). As a result, the decision depends on a case-by-case evaluation of each patient's specific and general risks of PONV. The risks include non-smoking status, the female gender, a history of motion sickness or PONV, and whether the patient is going to receive IV opioids. The risk is about 40%, and the patient's risk is 10%, 20%, 40%, 60%, or 80% of having PONV when 0, 1, 2, 3, and 4 predictors are present, respectively. It is impossible to assign a set of similar predictors to each patient because they can be different, and regarding the study, there is evidence that the risk factor was indeed controlled. Additionally, each of the patients had a risk score of more than forty per cent, which I consider high (Apfel et al., 1999).

An increase in the duration and concentration of volatile anaesthesia will lead to increases in the incidence of PONV, specifically in the initial postoperative phase of 2-6 hours. In addition, there is no difference between the incidence of PONV and any volatile

anaesthesia. It depends on duration and concentration (Maharjan & Bing, 2021). On the other hand, using opioids at high risk for PONV is attractive in reducing PONV (Massoth et al., 2021). Furthermore, propofol had antiemetic properties by decreasing synaptic signalling in the olfactory cortex, leading to decreased glutamate and aspartate release. From another perspective, propofol may directly inhibit the CTZ and vagal nuclei, which are firmly associated with nausea and vomiting (Lingle, 2019). Therefore, these results show only significant statistical differences but no clinical differences in sevoflurane concentration or total propofol.

Extending the operative duration by thirty minutes can raise the risk of PONV up to 60% (Shaikh et al., 2016), and all participants in our study achieved more than thirty minutes for the operative duration.

Vital signs revealed statistically significant variations in blood pressure between research groups, but there were no clinical differences because all readings fell within the normal range.

4.2 Postoperative Nausea and Vomiting

Each multimodal of antiemetics with a different mechanism reduces the risk of PONV by roughly 25% (Ma et al., 2022). In other words, none of the antiemetic medications currently available are effective in preventing PONV, particularly in high-risk PONV factor scores (Cao et al., 2017). Additionally, the Combination of four prophylactic antiemetic interventions is not enough to guarantee a reduction in the incidence of PONV with a certainty of less than 10% in high-risk patients with an initial risk level falling between 60 to 80% (Kranke et al., 2020).

In conclusion, since pharmacologic interventions have not been successful in eradicating the problem of PONV, researchers have also investigated the potential benefits of non-pharmacologic interventions such as p-6 Acupressure (Elvir-Lazo et al., 2020). However, some studies found that the risk of PONV decreased equally after stimulating the P6 acupoint and after administering anti-emetic drugs (Direkvand-Moghadam & Khosravi, 2013).

The study was carried out on 116 women patients who went through laparoscopic surgery

with general anesthesia. Four groups of participants were based on the intervention received. It's worth noting that during the 24 hours post-surgery, 82.1% of patients in the Combination group experienced no nausea or vomiting compared to 73.3% in the Acupressure group, 62.1% in Metoclopramide, and 37.9% in the Placebo group.

Metoclopramide enhances the gastrointestinal response by blocking gastric smooth muscle relaxation and selectively boosting gut cholinergic activity through its gastrokinetic properties. As a result, it also strengthens the tone of the lower oesophagal sphincter. Thus, it decreases the risk of aspiration (Kaur et al., 2019) by antagonizing the dopaminergic D2 receptor (Maharjan & Bing, 2021), 5HT3 receptors, also an agonist at 5HT4 receptors (Isola et al., 2024).

A10mg of metoclopramide is safe, especially from extrapyramidal side effects (Maharjan & Bing, 2021). It is considered an effective dose to mitigate PONV in patients undergoing surgical procedures with general anaesthesia(De Oliveira Jr et al., 2012). In the current study, the same dose was used.

The impact of the 10 mg metoclopramide group in reducing PONV revealed no difference when paralleled with the Placebo group. In addition, our results are different from a study involving 72 patients of both genders who had elective surgeries open appendectomy or LC, equally and randomly divided into three groups: An 8 mg dexamethasone group, 100 ml normal saline group, and 10 mg metoclopramide group. The results noted an insignificant difference in nausea and vomiting when comparing the dexamethasone group with the normal saline group, but there was a significant difference when comparing the dexamethasone group with the metoclopramide group. The results also showed a significant difference when comparing the normal saline group with the metoclopramide group (Al-Radeef et al., 2020).

This study compared the effectiveness of different treatments in preventing postoperative nausea and vomiting in female patients at moderate risk. One hundred twenty patients underwent laparoscopic surgery and were divided into four groups. The first group received a placebo of saline. The second group was given 8 mg of dexamethasone. The third group was administered 20 mg of metoclopramide. The final combination group received both 8 mg dexamethasone and 20 mg metoclopramide. Results showed

significant differences in rates of vomiting between groups. The highest rate occurred in the placebo group, with 17 patients (56.7%) experiencing vomiting. In contrast, only 6 patients (20%) vomited in both the combination group and the dexamethasone group. Rates of nausea also differed significantly between treatments. While 19 patients (63.3%) felt nauseous with the placebo, only 6 patients (20%) in the dexamethasone group and 5 patients (16.7%) in the combination group experienced nausea. The metoclopramide group had 10 patients (33.3%) with nausea. The severity of nausea also varied substantially between treatments. On a scale of 1 to 5, the combination group reported the lowest average severity of 1.05 ± 0.90. The placebo group had the highest average of 3.07 ± 1.34. Both the combination and dexamethasone groups relieved nausea more effectively than metoclopramide alone. Finally, the need for rescue antiemetics was much lower in the combination (6 patients, 20%) and dexamethasone (7 patients, 23.3%) groups than the placebo group (19 patients, 63.3%) (Alkaissi et al., 2017).

Acupressure involves exerting pressure on the P6 point found on the inner side of the forearm, which is positioned about three finger widths above the wrist crease between the long flexor tendons and roughly 6 centimetres above the wrist to relieve nausea and vomiting, relieves abdominal and chest congestion, helps reduce excitement and relaxes the mind, nausea, and motion sickness (Jin et al., 2020; Mobarakabadi et al., 2020). In addition, it is considered non-invasive, simple to apply, has no side effects or drug interactions, has a high level of patient acceptance, and is economical (Samad et al., 2003) against common pharmacological treatment, which is determined as costly and with potential side effect (Roehrich, 2016).

In the present study, the p-6 Acupressure group is effective in alleviating PONV with the incidence of PONV in p-6 Acupressure at 26.7% compared with the Placebo group at 62.1%, which is in contrast with a study of a randomized control trial undergoing laparoscopic cholecystectomy intervention group (n= 43) include a participant with the application of acupressure was at the wrist. The beads were fixed accurately to the position within the pericardium 6 point. In the Position of Placebo, the device was applied to the wrist of the 41 participants in the control group, and the beads applied to the dorsum of each of the hands of the two groups were similarly found to be fixed to the position within the pericardium 6 points. The current study is aligned with Placebo. Both

techniques were used similarly as in the Position of Point. However, these results differ from the present study due to the insignificant difference in PONV between the intervention and control group in PACU and at thirty minutes postoperative, 3 hours, and 6 hours postoperatively (Hamid et al., 2022).

In addition, a large multi-centre trial randomly assigned patients scheduled for gynaecological surgery under general anaesthesia to three groups. The first group received bilateral pressure on the P6 acupressure point (n=135), while the second group received pressure on unrelated points (n=139). A third reference group had no intervention (n=136). Results showed that 46% of the reference group experienced postoperative nausea and vomiting (PONV) compared to 38% of the unrelated point group and 33% of the P6 group, with the P6 difference reaching statistical significance. While applying pressure to unrelated points performed similarly to P6, directly aligning with prior work, the current study demonstrated that P6 acupressure specifically reduced PONV more than a nonspecific intervention. Overall, this well-designed study substantiates the efficacy of P6 acupressure in mitigating PONV for gynaecological surgeries (Alkaissi et al., 2002).

Although a quasi-experimental design with pre and post-tests was implemented to assess the impact of acupressure on diminishing nausea and vomiting following general anesthesia, involving 64 equally divided subjects into a control and treatment group aged 18 to 45 years old with ASA class I or II, BMI ranging from 18 to 25 kg/m^2 and Aldrete score of at least 8, the results yield mixed feelings. The intervention incorporated acupressure band application to P6 while the control received usual postoperative care; both were monitored for nausea using the Gordon scale. Some reported relief after acupressure, whereas others felt indifferent, noting the aetiology of nausea post-op stems from diverse triggers. Given the multifactorial origins and patient variable sensitivity, more research is warranted to substantiate acupressure for post-anesthetic queasiness.

The intervention included acupuncture performed by either the left or right hand, which was not near the harmed or infusion area if bruised, swollen, or fractured. Patients would then be reassessed for nausea and vomiting sensations after 30 minutes had passed from the treatment start. Findings revealed that there was a considerable shift in the rates of nausea and retching before versus after acupressure treatment for the experiment group

with p = 0.000 compared to only p = 0.057 for the control group receiving compression before and following their involvement. The disparity in responses pre- and post between the two groups was determined to be statistically significant (Ratnawati & Muntholib, 2019). This agrees with a randomized controlled experiment concerning laparoscopic cholecystectomy. One hundred and eleven feminine individuals were integrated and portioned into three assemblies: Group 1 had a plastic cap located at the P6 acupoint. Group 2 (Placebo) had a wristband with an analogous outward appearance yet without a cap. Group 3 was the Control group. The employment of an acupressure wristband on the P6 acupoint demonstrated benefits in patients who underwent laparoscopic cholecystectomy, reduced the chance of nausea between two to six hours, and reduced the severity of nausea during the second postoperative hour ($p < 0.05$). These results are in alignment with prior studies. The Acupressure and Placebo groups exhibited a statistically noteworthy variance pertaining to the prevalence of postoperative nausea in the post-anaesthesia care unit, word, aggregate 24-hour duration, and also the rigour of nausea in the post-anaesthesia care unit and complete 24-hour extent (Sahin et al., 2018).

In the current study, there is a significant difference between the Acupressure group and Placebo group in PACU, word and total 24 hours in contrast to the study found that no statistically significant between Acupressure to the P6 acupoint and non-acupoint ($p > 0.05$), so the effectiveness of the p-6 acupoint in alleviating postoperative nausea was not deemed clinically significant (Sahin et al., 2018).

The recent trial showed the Acupressure group was similarly effective as metoclopramide in preventing postoperative nausea and vomiting after strabismus surgery, concurring with prior evidence that Acupressure at point P-6, ondansetron at 0.15 mg/kg and metoclopramide at 0.2 mg/kg intravenously reduced instances of vomiting and nausea for patients aged 10 to 60 in the 24 hours after strabismus surgery. This double-blind, randomized, placebo-controlled prospective study found that while the three treatments all substantially lowered the rate of postoperative nausea and vomiting, there was no statistically significant difference between metoclopramide, Acupressure, and ondansetron with regards to occurrences of nausea and vomiting during the initial 24-hour postoperative period (Ebrahim Soltani et al., 2011).

Several recent studies have examined the effectiveness of P6 acupressure for postoperative nausea and vomiting, arriving at conclusions comparable to the present investigation. In contrast, the findings revealed an inconsequential difference between ondansetron and P-6 Acupressure stimulation in preventing postoperative nausea and vomiting following elective laparoscopic colorectal surgery. Here, 80 adult patients classified as ASA physical status II or III were randomly assigned to one of two groups in a single-blind manner through a lottery system. Those in Group A (n=40) received an intravenous dose of 0.15 mg/kg of ondansetron during the procedure, while Group B (n=40) received acupressure applied to the P6 acupoint 30 minutes prior to surgery. Additionally, both groups were administered 0.15 mg/kg of dexamethasone intravenously during the operation (Rehman et al., 2022).

The clinical trial involved ninety patients between twenty and sixty years old classified as ASA physical status class I or II who were scheduled for ear surgery requiring general anaesthesia. These participants were randomly divided into two equal groups. Group A received acupressure at the P6 acupuncture point while undergoing the procedure. Meanwhile, Group B was administered ondansetron at a dosage of 0.1 milligrams per kilogram immediately after endotracheal intubation. The researchers determined that P6 acupuncture proved nearly as effective as ondansetron in mitigating postoperative nausea and vomiting. Specifically, the rates of nausea and vomiting documented every six hours throughout the subsequent twenty-four hours did not significantly differ between the groups, as evidenced by a p-value exceeding 0.05 at all measurement intervals (Kumar, 2017). Thus, the present finding partially agreed with that study due to the use of another antiemetic agent.

Another study compared the effect of p-6 Acupressure alone against two pharmacological antiemetic agents in participants by using a randomized control trial shown that non-pharmacological method of P6 Acupressure, can effectively use to decrease early postoperative nausea and vomiting, same as dexamethasone and metoclopramide in the initial postoperative period for 59 adult female patients undergoing laparoscopic cholecystectomy which 16% of group p- 6 Acupressure bilateral and 14.8% of group dexamethasone 8 mg + metoclopramide 10 mg iv complained from nausea in the first hour after recovery. During 3rd hour, 12% of group p- 6 had Acupressure bilateral, and 7.4% of the other group complained of vomiting (Mohsin et al., 2022).

The results of the present study demonstrated that the Combination group (p-6 Acupressure plus metoclopramide) was just as effective as the p-6 Acupressure group. No prior research had compared the use of p-6 Acupressure plus metoclopramide to p-6 Acupressure alone in patients undergoing laparoscopic cholecystectomy surgery.

4.3 Postoperative Symptoms

This study indicated that the most often mentioned adverse effects were headache, exhaustion, and drowsiness, which were relatively mild in the case of the introduction of acupressure and/or acupressure in conjunction with metoclopramide. However, it showed lower occurrence than the Metoclopramide and Placebo group. Still, the difference remains statistically insupportable, which is close to Alkaissi's report about the scale of all symptoms falling with the use of p-6 Acupressure by females who were getting ready for gynaecological operation (Alkaissi et al., 2002).

Similar to the present findings, the study that employed Dexamethasone, metoclopramide, and their Combination conducted in female patients at moderate to high risk of PONV who underwent laparoscopic surgery found no significant postoperative side effects (Alkaissi et al., 2017).

4.4 Rescue antiemetic

In the first 24 hours after surgery, 4 patients 14.3% in the Combination group and 7 patients 23.3% in the Acupressure group needed rescue antiemetics, which is significantly lower compared to Placebo 15(51.7%) but insignificant compared to metoclopramide group 11(37.9%). On the contrary, Sahin et al. (2018) found that Acupressure on the P6 acupoint was not deemed to be clinically useful in high-risk postoperative nausea and vomiting in reducing postoperative vomiting, antiemetic medicine requirements, or pain, anxiety, or analgesic drug requirements ($P > 0.05$). Moreover, there is an insignificant difference between the Acupressure and Placebo groups for rescue antiemetic requirement in both groups with a similar frequency, with $P = 0.744$, in patients undergoing laparoscopic cholecystectomy (Hamid et al., 2022). There is also no discernible difference between the Placebo groups and p-6 Acupressure for rescue antiemetics in patients undergoing gynecological surgery (Alkaissi et al., 2002). In addition, there was an insignificant difference between Metoclopramide groups

13(43.3%) and Placebo 19(63.3%) p = 0.1237 for rescue antiemetic requirement in total 24 hours postoperatively in 120 female patients facing a moderate to high risk for PONV are set to undergoing laparoscopic surgery (Alkaissi et al., 2017).

4.5 Acupressure side effect

The incidence of side effects linked to p–6 Acupressure bands is relatively high and seems influenced by the band's size. Therefore, the current findings, which were somewhat similar to another study, may be resolved by producing bands of different sizes (Alkaissi et al., 2002).

4.6 Conclusion

The combination of 6 P Acupressure and Metoclopramide has not exhibited higher effectiveness for preventing nausea and vomiting post-laparoscopic surgery than using P 6 Acupressure alone. Treating both sides of P6 with an acupressure band can be perceived as an efficient and safe way of modern handling to avoid PONV after laparoscopy compared with Metoclopramide and Placebo.

4.7 Limitations

Un available different band sizes which could resolved the acupreesure side effect.

Data only collecting from one hospital due to diffecult transferring between the cities as a result of occupation and 7th october war.

4.8 Recommendation

The researcher recommends using P-6 Acupressure to reduce PONV for those at-risk zones and, in Combination with antiemetics, is recommended if the patient is in a high-risk zone to prevent further episodes.

P-6 Acupressure is easily learnt and taught and patients should be informed about its potential role and taught how to apply it for the management of PONV and in combination with metoclopramide in high risk patient .

Due to the limitation in determining the impact of p-6 Acupressure on pain relief in the current study, pain medication should be postoperatively given as a regular schedule

rather than waiting for the patient to complain about pain. Thus, further studies are warranted.

4.9 Implication of research

Caring for patients aims to ensure their well-being; thus, patients' perception of their recovery from a surgical operation may differ from their practitioner's judgment. That is why patient perspective measures have become relevant in treatment. The researcher investigated a sample of patients at moderate or high risk of PONV and found that applying p-6 Acupressure had improved the outcomes.

4.10 Further Research

This study recommends future research the following:

- To examine the effect of antiemetic class as 5-HT3 receptor antagonists compared with p-6 Acupressure in patients with high risk for PONV.
- To examine the efficacy of unilateral p-6 Acupressure compared with bilateral p-6 Acupressure.
- A study should be carried out to determine the effect of p-6 Acupressure on pain compared with pain medications.
- A study should be carried out on different population who at risk for PONV such as after chemotherapy

List of Abbreviations

Abbreviation	Meaning
ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CO_2	Carbon Dioxide
Cm	Centimetre (s)
CNS	Central Nervous System
CTZ	Chemoreceptor Trigger Zone
D2	Dopamine Type 2
GA	General Anesthesia
Hrs	Hours
5HT3	5-HydroxyTryptamine receptor-subtype-3
IV	Intravenous
Kg	Kilogram(s)
LC	Laparoscopic Cholecystectomy
Lt	Litres
Min	Minute
Ml	Milliliter (s)
Mg	Microgram (s)
Mm	Millimeter (s)
Nacl	Normal Saline
PACU	Post-Anesthetic Care Unit
PONV	Postoperative Nausea and Vomiting
VAS	Visual Analog Scale

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Appendices

Appendix A

Consent form

جامعه النجاح الوطنية

كليه الدراسات العليا

موافقه للاشتراك في البحث العلمي

انا طالبة من كليه الدراسات العليا من جامعه النجاح الوطنية تحت إشراف الدكتورة عائده القيسي نود اخذ الموافقة منك لمشاركتك في بحث علمي سريري سيجرى في مستشفى رفيديا الجراحي في نابلس . الرجاء أن تأخذوا الوقت الكافي لقراءة المعلومات التالية بتأن قبل أن تقرروا إذا كنتم تريدون المشاركة في الدراسة أم لا . بإمكانكم طلب إيضاحات أو معلومات إضافية عن أي شيء مذكور في هذه الاستمارة أو عن هذه الدراسة من الباحث.

عنوان الدراسة :

منع الغثيان والقيء بعد الجراحة في المرضى الإناث الذين خضعوا لجراحة استئصال المرارة بالمنظار باستخدام البرامين وحده مقابل البرامين جنبًا إلى جنب مع تحفيز العلاج بالضغط على-P 6

الهدف من الدراسة :

دراسة مدى فعالية دواء البرامين لوحده او مع تحفيز العلاج بالضغط على P-6 للوقاية من الغثيان والقيء بعد الجراحة الاناث المرضى الذين يخضعون لجراحة استئصال المرارة بالمنظار

فتره المشاركة في الدراسة :

تبدأ مشاركتك في الدراسة قبل بدأ العملية الجراحية المخطط لها ب 30 دقيقه ومراقبه حالتك الصحية حتى مدة اربعة وعشرون ساعه من العملية .

إجراء الدراسة :

سيتم توزيع المشاركين في الدراسة إلى اربعه مجموعات بطريقه عشوائية ، حيث تتلقى المجموعة الأولى علاج " البرامين " في قبل البدء بالتخدير مع active p-6 Acupressure، والمجموعة الثانية سوف تتلقى علاج وهمي مع active p-6 Acupressure والمجموعة الثالثة سوف تتلقى علاج البرامين في قبل البدء بالتخدير مع inactive p-6 Acupressure والمجموعه الرابعة سوف تتلقى علاج وهمي مع inactive p-6 Acupressure

الفوائد المتوقعة للمشاركة في الدراسة :

تخفيف المضاعفات المحتمل حدوثها بعد العملية (الغثيان والتقيؤ) .

التأثيرات السلبية للمشاركة في الدراسة :

التأثيرات المتوقعة هي من الأعراض الجانبية للأدوية ، لذلك الأدوية سوف تعطى في جرعات خفيفة ولمرة واحده فقط مما يقلل من الأعراض الجانبية لها ، وفي حال حدوث هذه الأعراض سيتم تقديم العلاج المناسب لها بغض النظر في أي مجموعه انت .

سريه المعلومات :

لحماية خصوصيتك ، سوف يتم تسجيل النتائج مع رمز سري . سوف يتم تسجيل فقط اسمك في نموذج الموافقة وسيتم الإبقاء على رمز السري المعين في ملف مغلق ومحمي بعناية وسيكون الوصول لهذه المعلومات يتم فقط من قبل الباحث الرئيسي للدراسة والأفراد المرخص لهم . مع ذلك، قد تتم مراجعه سجلات الدراسة من قبل اللجنة الأخلاقية التي تجري على البشر في جامعه النجاح الوطنية. ستتم مراقبه السجلات الخاصة بك ويمكن مراجعتها دون انتهاك السرية وأيه بيانات يمكن أن تنتج عن هذه الدراسة لن تذكر أسماء المشاركين في الدراسة.

المشاركة الطوعية/ الانسحاب :

إن مشاركتك في هذه الدراسة طوعيه تماما، يمكنك سحب موافقتك في أي وقت . وإذا اخترت عدم مشاركه في الدراسة أو الانسحاب في وقت لاحق من هذه الدراسة لن تتأثر الرعاية الطبية المقدمة لك أو تتغير بأي شكل من الأشكال. إذا كنت ترغب بالانسحاب من الدراسة، يمكننك الاتصال بالباحث .

الاتصال للحصول على أجوبه على أسئلتك ومخاوفك وشكوك :

إذا كان لديكم أي أسئلة، مخاوف أو شكاوي، يرجى الاتصال بالباحث للدراسة على الرقم المدرج أسفل الصفحة من هذه الموافقة .

الموافقة على المشاركة في الدراسة :

لقد قرأنا الوصف أعلاه من هذه الدراسة وقد تمت الإجابة على جميع أسئلتنا . ونحن نعلم بإمكاننا ان نرفض مشاركه او الانسحاب من الدراسة في أي وقت وعلى ذلك نعطي موافقة بحريه للمشاركه في هذه الدراسة .

الباحث رقم الهاتف

دانا كمال عبد العزيز العويصات 0568743087

اسم المشارك في البحث :

التوقيع :

التاريخ :

Appendix B

Collecting Data Sheet

Demographic data

Name	
Age (year)	
History of PONV in previous operation (Yes/NO)	
History of motion sickness (Yes/No)	
Planning for Opioid use postoperatively (Yes/No)	
Smoking (Yes/No)	
Apfel simplified risk score for PONV (%) 1 factor: 20% 2 factor:40% 3 factor: 60% 4 factor: 80%	
Weight (kg)	
Height (Cm)	
BMI	

Surgical variables

Total fentanyl (µg)	
Total propofol (mg)	
End-tidal isoflurane concentration, %	
End-tidal CO2, mmHg	
Duration of surgery	
Duration of anesthesia	
Intraoperative fluid intake	
Intraoperative FIO	

Intraoperatively

Variable	15 min	30min	45 min	60 min	75 min	90	105	120
Systolic BP								
Diastolic BP								
MAP								
Respiratory rate								
SPO2								

Postoperatively

Variable	On arrival
Systolic BP	
Diastolic BP	
MAP	
Respiratory rate	
SPO2	

In the ward

Variable	On arrival	6th hour	12th hour	24th hour
Systolic BP				
Diastolic BP				
MAP				
Respiratory rate				
SPO2				
Intraoperative fluid intake, ml				

In PACU

Variable	On arrival
Incidence of nausea Yes/no	
Intensity of nausea 0-6	
Incidence of vomiting (yes/No)	
Antiemetic rescue medication dexamethasone 8 mg	
Incidence of headache (yes/No)	
Incidence of fatigue (yes/No)	
Incidence of drowsiness (yes/No)	
Incidence blurred vision (yes/No)	
Incidence of constipation (yes/No)	
Incidence of diarrhea (yes/No)	
Extrapyramidal symptom (Yes/No)	

In the surgical ward

Variable	On arrival	6th hr.	12th hr.	24th hr.
Incidence of nausea Yes/no				
Intensity of nausea 0-6				
Incidence of vomiting (yes/No)				
Antiemetic rescue medication metoclopramide 10 mg (i.v)				
Incidence of headache (yes/No)				
Incidence of fatigue (yes/No)				
Incidence of drowsiness (yes/No)				
Incidence blurred vision (yes/No)				
Incidence of constipation (yes/No)				
Incidence of diarrhea (yes/No)				
Extrapyramidal symptom (Yes/No)				
Duration of hospital stay				

Acupressure PACU

Variable	30 min before surgery	On arrival
Mild discomfort (yes/No)		
Swollen wrists (yes/No)		
Redness (yes/No)		
Skin breakdown Near wristband (yes/No)		
Itching (yes/No)		

Acupressure in the surgical ward

Variable	On arrival	6th hr.	12th hr.	24th hr.
Mild discomfort (yes/No)				
Swollen wrists (yes/No)				
Redness (yes/No)				
Skin breakdown Near wristband (yes/No)				
Itching (yes/No)				

Satisfaction of PONV management

Variable*choose one of the following	
very unsatisfied	
Unsatisfied	
neither satisfied nor unsatisfied	
Satisfied	
very satisfied	

Appendix C

IRB form

An-Najah National
University
Faculty of Medicine &
Health Sciences
Institutional Review Board

جامعة النجاح الوطنية
كلية الطب وعلوم الصحة
لجنة اخلاقيات البحث العلمي

Ref: Mas . May. 2023/12

IRB Approval Letter

Title of Research:

Preventing postoperative nausea and vomiting in female patients having laparoscopic cholecystectomy surgery with metoclopramide alone vs. metoclopramide combined with P-6 Acupressure stimulation

Submited by:
Dana Kamal Ewesat

Supervisor:
Aidah Alkaissi

Approved:
10th May. 2023

Your Study Title **"Preventing postoperative nausea and vomiting in female patients having laparoscopic cholecystectomy surgery with metoclopramide alone vs. metoclopramide combined with P-6 Acupressure stimulation,"** reviewed by An-Najah National University IRB committee and was approved on 10th, May . 2023

Hasan Fitian, MD

IRB Committee Chairman

IRB
Institutional Review Board

Nablus - P.O Box :7 or 707 | Tel (970) (09) 2342902/4/7/8/14 | Faximile (970) (09) 2342910| E-mail : IRB@najah.edu

Appendix D

Computerized Random Sequence Generator

Random Sequence Generator

Here is your sequence:

6	87	120	10
4	103	73	98
96	7	32	24
44	114	72	18
66	99	12	26
34	76	63	108
16	65	81	1
75	35	84	88
109	80	37	17
110	85	83	29
13	33	31	77
68	69	53	86
101	61	79	111
89	91	117	58
70	20	71	90
27	97	11	104
50	52	62	113
21	41	49	15
51	55	107	22
36	100	112	43
56	48	45	119
40	93	74	30
46	60	59	38
42	2	64	5
105	47	116	19
9	118	57	3
115	67	8	106
102	78	28	39
95	23	82	25
92	54	94	14

Appendix E

Certificate of English Proofreading and Editing

Certificate of English Proofreading and Editing

This certificate confirms that the thesis mentioned below was proofread by an expert in academic English and edited by a native speaker.

The following issues were corrected: grammar, punctuation, sentence structure, and phrasing.

Faculty of Graduate Studies at An-Najah National University can contact us for a copy of the edited document that the author submitted.

Title

Preventing Postoperative Nausea and Vomiting in Female Patients Having Laparoscopic Cholecystectomy Surgery with Metoclopramide Alone Vs. Metoclopramide Combined with P-6 Acupressure Stimulation

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Appendix F

Tables

Table 11

The numbers and percentage of episodes of postoperative symptoms in the study groups of patients in PACU, Ward, and in the total 24 hours postoperatively

Variable	Group				P-value
	Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	
Incidence of headache (In PACU)	2(7.1%)	5(16.7%)	9(31%)	7(24.1%)	0.130
Incidence of headache (In Ward)	6(21.4%)	4(13.3%)	9(31%)	7(24.1%)	0.436
Incidence of headache (In Total 24 hrs.)	7(25%)	6(20%)	11(37.9%)	7(24.1%)	0.441
Incidence of fatigue (In PACU)	4(14.3%)	9(30%)	14(48.3%)	10(34.5%)	0.052
Incidence of fatigue (In Ward)	8(28.6%)	9(30%)	12(41.4%)	10(34.5%)	0.732
Incidence of fatigue (In Total 24 hrs.)	9(32.1%)	9(30%)	14(48.3%)	10(34.5%)	0.463
Incidence of drowsiness (In PACU)	6(21.4%)	10(33.3%)	12(41.4%)	12(41.4%)	0.341
Incidence of drowsiness (In Ward)	8(28.6%)	8(26.7%)	9(31%)	12(41.4%)	0.630
Incidence of drowsiness (In Total 24 hrs.)	9(32.1%)	10(33.3%)	13(44.8%)	12(41.4%)	0.706
Incidence of blurred vision (In PACU)	0(0%)	0(0%)	1(3.4%)	0(0%)	0.388
Incidence of blurred vision (In Ward)	0(0%)	1(3.3%)	1(3.4%)	0(0%)	0.579
Incidence of blurred vision (In Total 24 hrs.)	0(0%)	1(3.3%)	1(3.4%)	0(0%)	0.579
Incidence of constipation (In PACU)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Incidence of constipation (In Ward)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Incidence of constipation (In Total 24 hrs.)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Incidence of diarrhea (In PACU)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Incidence of diarrhea (In Ward)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Incidence of diarrhea (In Total 24 hrs.)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Extrapyramidal symptom (In PACU)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Extrapyramidal symptom (In Ward)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Extrapyramidal symptom (In Total 24 hrs.)	0(0%)	0(0%)	0(0%)	0(0%)	-----

Note: Significant at 0.05, Data are Mean ±SD with P-values derived from one-way ANOVA, Frequencies, and Percentages (%) with P-values derived from the Chi-Square test.

Table 12

The numbers and percentage of rescue antiemetics between the study groups of patients in PACU, Ward, and in the total 24 hours postoperatively

Variable	Group Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	P-value
Rescue antiemetic (In PACU)	1(3.6%)	4(13.3%)	9(31%)	15(51.7%)	0.000
Rescue antiemetic (In Ward)	3(10.7%)	5(16.7%)	4(13.8%)	7(24.1%)	0.557
Rescue antiemetic (In Total 24 hrs.)	4(14.3%)	7(23.3%)	11(37.9%)	15(51.7%)	0.013

Note: Significant at 0.05, Data are Mean ±SD with P-values derived from one-way ANOVA, Frequencies, and Percentages (%) with P-values derived from the Chi-Square test.

Table 13

Frequency comparison for significant rescue antiemetic between study groups in PACU and in total 24 hours

Variable	Group Combination (A)	Acupressure (B)	Pramin (C)	Placebo (D)
Rescue antiemetic (In PACU)	----	----	A	A B
Rescue antiemetic (In Total 24 hrs.)	----	----	----	A B

Note: Significant at 0.05, Post-hoc pairwise mean comparisons test adjusted using the Bonferroni correction.

Table 14

The numbers and percentage of Acupressure side effects between the study groups of patients in PACU, Ward, and in the total 24 hours postoperatively.

Variable	Group				
	Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	P-value
Mild discomfort (In PACU)	2(7.1%)	5(16.7%)	5(17.2%)	7(24.1%)	0.386
Mild discomfort (In Ward)	6(21.4%)	11(36.7%)	8(27.6%)	10(34.5%)	0.580
Mild discomfort (In Total 24 hrs.)	6(21.4%)	11(36.7%)	8(27.6%)	10(34.5%)	0.580
Swollen wrists (In PACU)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Swollen wrists (In Ward)	0(0%)	5(16.7%)	5(17.2%)	0(0%)	0.014
Swollen wrists (In Total 24 hrs.)	0(0%)	5(16.7%)	5(17.2%)	0(0%)	0.014
Redness (In PACU)	0(0%)	5(16.7%)	4(13.8%)	3(10.3%)	0.180
Redness (In Ward)	7(25%)	6(20%)	6(20.7%)	8(27.6%)	0.888
Redness (In Total 24 hrs.)	7(25%)	7(23.3%)	6(20.7%)	8(27.6%)	0.941
Skin breakdown near wristband (In PACU)	0(0%)	2(6.7%)	1(3.4%)	0(0%)	0.310
Skin breakdown near wristband (In Ward)	1(3.6%)	5(16.7%)	5(17.2%)	1(3.4%)	0.130
Skin breakdown near wristband (In Total 24 hrs.)	1(3.6%)	5(16.7%)	5(17.2%)	1(3.4%)	0.130
Itching (In PACU)	0(0%)	0(0%)	0(0%)	0(0%)	-----
Itching (In Ward)	0(0%)	2(6.7%)	2(6.9%)	6(20.7%)	0.041
Itching (In Total, 24 hrs.)	0(0%)	2(6.7%)	2(6.9%)	6(20.7%)	0.041

Note: Significant at 0.05, Data are Mean ±SD with P-values derived from one-way ANOVA, Frequencies, and Percentages (%) with P-values derived from the Chi-Square test.

Table 15

Frequency comparison for significant Acupressure side effects between study groups in Ward and in Total 24 hours

Variable	Group			
	Combination (A)	Acupressure (B)	Pramin (C)	Placebo (D)
Swollen wrists (In Ward)	----	AD	AD	----
Swollen wrists (In Total 24 hrs.)	----	AD	AD	----
Itching (In Ward)	----	----	----	A
Itching (In Total 24 hrs.)	----	----	----	A

Note: Significant at 0.05, Post-hoc pairwise mean comparisons were adjusted using the Bonferroni correction.

Table 16

The numbers and percentages of patient reports regarding satisfaction

Variable	Group				P-value
	Combination (N=28)	Acupressure (N=30)	Pramin (N=29)	Placebo (N=29)	
Are you satisfied with the treatment that was given to you?					
Very Unsatisfied	0(0%)	3(10%)	2(6.9%)	6(20.7%)	
Unsatisfied	2(7.1%)	3(10%)	3(10.3%)	3(10.3%)	
Neither satisfied nor unsatisfied	2(7.1%)	3(10%)	3(10.3%)	2(6.9%)	0.017
Satisfied	7(25%)	13(43.3%)	10(34.5%)	8(27.6%)	
Very satisfied	17(60.7%)	8(26.7%)	11(37.9%)	10(34.5%)	

Note: Significant at 0.05, Data are Mean ±SD with P-values derived from one-way ANOVA, Frequencies, and Percentages (%) with P-values derived from the Chi-Square test.

جـامعـــة النجاح الوطنية
كليـــة الدراســـات العليـــا

منع الغثيان والقيء بعد الجراحة في المرضى الإناث الذين خضعوا لجراحة استئصال المرارة بالمنظار باستخدام البرامين وحده مقابل البرامين جنبًا إلى جنب مع تحفيز العلاج بالضغط على P-6

إعداد
دانا العويصات

إشراف
د. عايدة القيسي

قدمت هذه الرسالة استكمالا لمتطلبات الحصول على درجة الماجستير في تمريض التخدير، من كلية الدراسات العليا، في جامعة النجاح الوطنية، نابلس– فلسطين.

2024

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اعداد
دانا العويصات
اشراف
د. عايدة القيسي

الملخص

تشير الأدلة إلى الأهمية المحتملة للعلاجات غير الدوائية في الوقاية من القيء والغثيان بعد العملية في المرضى المعرضين لمخاطر عالية و السبب انه لا يوجد مضاد للقيء فعال في تقليل الغثيان والقيء بعد العملية الجراحية، على الرغم من الأبحاث المكثفة. من أجل منع القيء والغثيان في المرضى الإناث الذين يخضعون لعمليات جراحية بالمنظار تحت التخدير العام، تبحث هذه الدراسة في فعالية ميتوكلوبراميد بمفرده أو مع العلاج بالضغط على P-6.

تم توزيع مائة وستة عشر مريضة الى اربع مجموعات في تجربة عشوائية صارمة مستقبلية مزدوجة التعمية خاضعه للعلاج الوهمي حيث تلقت مجموعة الدمج (العدد = 28) التي تلقت مزيجًا من العلاج بالضغط على P−6 قبل 30 دقيقة من التخدير و10 ملغم من ميتوكلوبراميد قبل دقيقة واحدة من بدء التخدير، و مجموعة العلاج بالضغط (العدد = 30) التي تلقت العلاج بالضغط على p-6 و1 مل نورمال، ومجموعة البرامين (العدد = 29) التي تلقت 10 ملغم من ميتوكلوبراميد والعلاج الوهمي بالضغط قبل 30 دقيقة من التخدير، ومجموعة العلاج الوهمي (العدد = 29) التي تلقت العلاج الوهمي بالضغط و1 مل نورمال سلاين قبل دقيقه واحده من بدء التخدير. وتم تقييم الأعراض ما بعد العملية الجراحية.

هناك فروق إحصائية في حدوث القيء خلال 24 ساعة بعد العملية ($p < 0.001$) بين مجموعة الدمج 44.3%، مجموعة العلاج بالضغط 20%، مجموعة البرامين 11.9%، ومجموعة الدواء الوهمي 17.6%.

تم استخدام اختبار ما بعد المخصص و لوحظ وجود فرق إحصائي بين المجموعتين الدمج والعلاج الوهمي، وكذلك بين المجموعتين الدمج والبرامين. كما لوحظ فروق احصائية في حدوث الغثيان بعد 24 ساعة من الجراحة بين العلاج بالضغط 26.7% والدمج 17.9% مقارنة بمجموعة العلاج الوهمي 62.1%، P. 0.05> وبعد 24 ساعة فقط من الجراحة، كانت هناك فروق احصائية في شدة الغثيان بين مجموعة الدمج (0.17) ومجموعة العلاج الوهمي (0.81)، بقيمة p 0.006 وذلك خلال فترة 24 ساعة بأكملها، مقارنة بمجموعة العلاج الوهمي 51.7%، ومجموعة الدمج 14.3% ومجموعة العلاج بالضغط 23.3% لديها معدلات استخدام أقل بكثير لمضادات القيء، P <0.05.

في المرضى الإناث الذين يخضعون لعملية جراحية بالمنظار، فإن الميتوكلوبراميد بالإضافة إلى استخدام العلاج بالضغط على p-6 يقلل بشكل كبير من حدوث وشدة القيء والغثيان بعد العملية وكذلك تقليل الحاجة الى استخدام مضادات مما يجعله نهجًا وقائيًا أقوى من أي دواء بمفرده.

الكلمات المفتاحية: الجراحة بالمنظار، العلاج بالضغط على p-6 ، ميتوكلوبرمايد، القيء والغثيان بعد العملية، العلاجات غير دوائية.