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Flem-Flam Aaron Flemister  
*University of Southern Mississippi*

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The University of Southern Mississippi

A PILOT STUDY OF PROPOFOL AS AN ANTI-EMETIC IN LAPAROSCOPIC,  
GYNECOLOGIC SURGERY PATIENTS

by

Flem-Flam Aaron Flemister

Abstract of a Capstone Project  
Submitted to the Graduate School  
of the University of Southern Mississippi  
in Partial Fulfillment of the Requirements  
for the Degree of Doctor of Nursing Practice

December 2015

## ABSTRACT

### A PILOT STUDY OF PROPOFOL AS AN ANTI-EMETIC IN LAPAROSCOPIC, GYNECOLOGIC SURGERY PATIENTS

by Flem-Flam Aaron Flemister

December 2015

The goal of this project was to use sub-hypnotic doses of propofol to decrease postoperative nausea and vomiting (PONV) rates in the immediate post-operative period in females, ages 18-65, undergoing laparoscopic gynecologic surgery.

PONV is one of the largest complications of anesthesia affecting 20-30% of all surgical patients. Risk factors associated with PONV are female gender, laparoscopy, general anesthesia, opioids, volatile agents, and post-operative pain; all of which are frequently encountered. The incidence of PONV can prolong recovery time, delay discharge, increase patient cost, decrease patient satisfaction, and can cause significant medical complications. Propofol has previously demonstrated anti-emetic properties; often being used in total intravenous anesthesia in patients with known PONV.

This pilot study investigated if the administration of a sub-hypnotic dose of propofol, as an anti-emetic during emergence period of anesthesia, affects PONV rates during the immediate post-operative period. A randomized, blinded, controlled comparison group study was conducted to investigate the use of propofol as an antiemetic. A group of 10 (N=10) ASA I or II patients, aged 18-65, undergoing laparoscopic, gynecologic surgery were examined using a verbal analog scale. These patients were randomly assigned to a control group which received Zofran™ only, or a treatment group which received Zofran™ and propofol.

A paired samples t-test failed to reveal a statistically reliable difference between the mean of the CX ( $M = 0$ ,  $s = 0$ ) and TX ( $M = 2.00$ ,  $s = 4.472$ ) group created during this pilot study,  $t(8) = 1.000$ ,  $p = .0174$ ,  $\alpha = .05$ . A chi-square test was performed and no relationship was found between the CX and TX groups in relation to vomiting,  $\chi^2(1, N = 10) = 1.111$ ,  $p = 0.146$ . Thus, the pilot study determined there was no statistical significance of preventing PONV with sub-hypnotic doses of propofol.

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2015

A PILOT STUDY OF PROPOFOL AS AN ANTI-EMETIC  
IN LAPAROSCOPIC, GYNECOLOGIC SURGERY

by

Flem-Flam Aaron Flemister

A Capstone Project  
Submitted to the Graduate School  
and the Department of Advanced Practice  
at The University of Southern Mississippi  
in Partial Fulfillment of the Requirements  
for the Degree of Doctor of Nursing Practice

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December 2015

## DEDICATION

I would first like to give the glory to God in that He walked with me through this whole process. I would like to extend my gratitude to my parents, family, and friends for their support during this journey of earning this doctoral degree. Thank you for your patience and support during this milestone.

## ACKNOWLEDGMENTS

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## LIST OF ABBREVIATIONS

<i>5HT</i>	5-hydroxytryptamine
<i>ASA</i>	American Society of Anesthesiologists
<i>ASC</i>	Ambulatory Surgical Center
<i>BSO</i>	Bilateral Salpingo-Oophorectomy
<i>CN</i>	Cranial Nerve
<i>CRNA</i>	Certified Registered Nurse Anesthetist
<i>CRTZ</i>	Chemoreceptor Trigger zone
<i>CSF</i>	Cerebral Spinal Fluid
<i>EBL</i>	Estimated Blood Loss
<i>EBP</i>	Evidenced Base Practice
<i>FDA</i>	Food and Drug Administration
<i>GABA</i>	Y-aminobutyric acid
<i>IRB</i>	Institutional Review Board
<i>LAVH</i>	Laparoscopic Assisted Vaginal Hysterectomy
<i>LR</i>	Lactated Ringer
<i>MAC</i>	Minimum alveolar concentration
<i>ML</i>	Milliliters
<i>OB/GYN</i>	Obstetrics/Gynecology
<i>OR</i>	Operating Room
<i>PACU</i>	Post Anesthesia Care Unit
<i>PONV</i>	Post-Operative Nausea and Vomiting
<i>PS</i>	Physical Status

*SPSS*

Statistical Software for Social Sciences

*VC*

Vomiting Center

## CHAPTER I

### INTRODUCTION

#### Background

Postoperative nausea and vomiting was first identified in surgical patients in 1914 and remains a major complication of anesthesia (Butterworth, Mackey, & Wasnick, 2013; Forren, 2014). It is predicted that PONV affects 20-30% of all surgical patients (Butterworth et al., 2014). Risk factors often related with PONV are female gender, laparoscopy, general anesthesia, opioids, volatile agents, and post-operative pain (Butterworth et al., 2013). However, all of these risk factors are frequently encountered in the clinical setting (Butterworth et al., 2013). As research has evolved, a commonly-used anesthetic, propofol, has been identified to have antiemetic properties when used as an induction agent or supplemental intravenous anesthetic (Forren, 2014).

#### Clinical Question

In adult female patients undergoing laparoscopic gynecologic surgeries, how does the administration of a sub-hypnotic dose of propofol, as an anti-emetic at extubation, affect PONV rates during the immediate post-operative period? This research question entails many variables that were examined individually in regards to the treatment of PONV in the selected surgical population.

#### Problem Statement

The experience of PONV can decrease satisfaction scores of the patient and can also account for a loss of revenue (Prevention of PONV, 2013; Thompson, 1999). The incidence of PONV can cause a financial loss of approximately \$415 per patient, related to increased personnel time, supplies, and drugs (Prevention of PONV, 2013; Thompson,

1999). Many other complications can develop as a result of PONV such as: increased anxiety, decrease in oxygen saturation level, hypovolemia, electrolyte imbalances, incisional pain, increased risk of incisional dehiscence, increased intracranial pressure, risk of aspiration, and many other complications (DeLeskey, 2009; Forren, 2014; Prevention of PONV, 2013; Thompson, 1999).

These complications are not only harmful to the patient, but can increase post-operative recovery time. The incidence of PONV can also cause increased patient utilization of the post-anesthesia recovery unit (PACU) (DeLeskey, 2009; Prevention of PONV, 2013; Thompson, 1999). An increase in PACU time can cause a delay in the operating room schedule due to the limited availability of recovery room beds (Thompson, 1999). During development of the solution to the identified clinical problem of PONV, these variables were accounted for in the proposed plan to increase curiosity of the sponsoring organization.

#### Purpose of Project

While recognized as a common complication of anesthesia for many decades, PONV remains a notable clinical problem of anesthesia practice (DeLeskey, 2009; Hambridge, 2012; Thompson, 1999). Among patients that have multiple risk factors, or are considered high-risk patients, PONV incidence can be as high as 70% (Deleskey, 2009; Hambridge, 2012). Laparoscopic procedures increase the frequency of PONV due to insufflation of the abdomen and bowel manipulation (Butterworth et al., 2013; Joshi & Cunnigham, 2013; Pawar, Sarkar, & Dewoolkar, 2009). Thus, laparoscopic surgical patients were identified as a high-risk patient population for PONV, and the



recommendation is to implement a multimodal antiemetic approach in this population (Joshi & Cunnigham, 2013).

The goal of this project was to use of sub-hypnotic doses of propofol to decrease PONV rates in the immediate post-operative period in females undergoing laparoscopic, gynecologic surgery. By decreasing the rates of PONV, potential complications can be avoided, and patient satisfaction will increase. The goal was an improvement in patient outcomes following laparoscopic, gynecologic surgery through the implementation of the selected intervention,

#### Needs Assessment

PONV is a common complication of anesthesia, with an incidence of 20-30% and requires prevention and treatment measures by the anesthesia provider (Butterworth, Mackey, & Wasnick, 2013; Forren, 2014). By decreasing the rate of PONV, patient satisfaction will increase, patient outcomes will improve, facility costs will decrease, and the surgical center can have higher productivity. In implementing a clinical protocol to decrease PONV by administering sub-hypnotic doses of propofol in addition to Zofran™, the purpose was to determine if this intervention improved patient outcomes by decreasing the rate of PONV in the immediate post-operative period. While the decreased rates of PONV will be the main goal in this project, financial consideration was also examined to determine if there was a cost savings or higher expense with the intervention.

Effectively preventing and treating PONV not only increases patient safety and satisfaction, but also increases the efficiency and productivity of the operating room (OR) and PACU (Fombour et al., 2002; Thompson, 1999). Increasing proficiency and

productivity were a strength of the intervention, which helped to encourage buy-in by the clinical facility. The incidence of PONV cannot only decrease satisfaction scores of the patient affecting their view of the quality of care they received, but can also account for a loss of revenue (Thompson, 1999).

Therefore, by using propofol as an antiemetic, increased patient satisfaction and decreased healthcare costs could theoretically improve due to decreasing incidence of PONV. However, achieving the appropriate balance between the dosage of the sub-hypnotic doses of propofol and the effectiveness of PONV prevention is necessary for cost-effective care. The weakness of the intervention implementation was a perceived increased cost of care associated with the use of propofol as an antiemetic.

An opportunity for this study was the desire by the ambulatory surgery center (ASC) or hospital to improve patient outcomes and decrease discharge time. This desire allowed the study to try to achieve these goals by decreasing PONV rates and recovery times in the PACU. A threat, however, was the approval process and cooperation of the center's staff in the implementation of the clinical project. Without the support and participation of the clinical staff, the study would not have been complete.

In developing the research question, adult female patients undergoing laparoscopic gynecologic procedures were identified as the target population. Female patients undergoing gynecologic laparoscopic surgery are at an increased risk of PONV due to: female gender, laparoscopic surgery, intra-abdominal surgery and post-operative pain; which are all considered risk factors for PONV (Butterworth et al., 2013; Joshi & Cunningham, 2013). The additive result of each risk factor for PONV in this population places them at an even higher risk for PONV, which means they have a 70% possibility

of developing the complication (Deleskey, 2009). It has been reported that gynecologic surgeries carry the highest risk for PONV with an incidence of 60-83% in this patient population (Ramanathan, Augustus, Thiruvengadam, Sundaram, & Deepalakshmi, 2003). Further, the majority of gynecologic surgeries are now being performed on an outpatient basis. Outpatient surgery requires the provider to prevent effectively or quickly provide treatment for PONV for rapid discharge from the surgery center (Ramanathan et al., 2003).

## CHAPTER II

### REVIEW OF RELATED LITERATURE

Since being first identified in scholarly publication in 1914, postoperative nausea and vomiting (PONV) is still one of the most frequent complication of anesthesia (Butterworth et al., 2013). PONV is estimated to affect 20-30% of all surgical patients (Butterworth et al., 2013). PONV is a complication of anesthesia that is not only undesirable, but also delays recovery in the post anesthesia care unit (PACU) (Borgeat, Wilder-Smith, Saiah, & Rifat, 1992; Gan et al., 1996; Lambert, Wakim, & Lambert, 2009; Thompson, 1999). The complication of PONV also decreases patient comfort, delays discharge home, and can result in more serious complications such as aspiration pneumonia or surgical wound dehiscence (Borgeat, Wilder-Smith, Saiah, & Rifat, 1992; Gan et al., 1996; Lambert, Wakim, & Lambert, 2009; Thompson, 1999). Even as anesthesia techniques and equipment have improved drastically from the period of ether anesthesia, PONV still occurs with high frequency (Gan et al., 1996; Lambert et al., 2009). PONV is estimated to have an incidence of 25-30% for all surgeries, with up to 70% in high-risk patients such as women undergoing gynecological surgery (Butterworth et al., 2013; Kovac, 2000; Kovac, 2006; Lambert et al., 2009; Thompson, 1999).

#### PONV Mechanism

PONV is a common occurrence in anesthesia, partly due to the narcotic agents that are used during the procedures for pain control (Lambert et al., 2009). While PONV is often multifactorial in development, it is often caused by the stimulation of the chemoreceptor trigger zone (CRTZ) which lies in the fourth ventricle of the brain (Lambert et al., 2009; Norred, 2003; Thompson, 1999). Nausea initiates in the CRTZ

due to its locations in the area postrema below the fourth ventricle and the solitary tract nucleus (Sharkey & Wallace, 2011; Watcha & White, 1992). The highly vascularized CRTZ area has no blood-brain barrier; allowing reaction to substances in the blood and cerebral spinal fluid (CSF) (Pellegrini, Deloge, Bennett, & Kelly, 2009; Sharkey & Wallace, 2011; Thompson, 1999; Watcha & White, 1992). The CTRZ has receptor sites for dopamine, opioids, serotonin, and enkephalins (Kovac, 2000; Norred, 2003; Sharkey & Wallace, 2011, Watcha & White, 1992). Additionally, histaminic and muscarinic cholinergic receptors that can be stimulated by substances in the blood, and CSF are located in the CTRZ (Kovac, 2000; Norred, 2003; Sharkey & Wallace, 2011, Watcha & White, 1992).

The stimulation of the receptors in the CRTZ often are initiated by periphery components such as the oropharynx, gastrointestinal tract, peritoneum, and genitalia (Thompson, 1999). However, central stimulation of the vestibular apparatus, cerebral cortex, or labyrinthine can also stimulate nausea and vomiting (Thompson, 1999). Nausea is excitation of the CTRZ and vomiting center, which can occur by: “irritative impulses coming from the gastrointestinal tract, impulses that originate in the lower brain associated with motion sickness or impulses from the cerebral cortex to initiate vomiting” (Hall & Guyton, 2011, p. 804). The CTRZ communicates central cerebral stimuli to the vomiting center (VC) (Kovac, 2000). The VC receives inputs from “multiple afferent sensory pathways including cranial nerve (CN) X the vagus nerve, CN VIII the vestibular nerve, the limbic system and the CRTZ” (Thompson, 1999, p. 1131). Since the CTRZ is the area that comprises of the receptors that cause PONV, this area was the focus of this

study. Nausea is considered a protective reflex and is subjective to the patient; nausea can be experienced alone or in conjunction with vomiting or retching (Kovac, 2000).

Vomiting or retching can sometimes follow nausea stimulus. Vomiting, or emesis, is a method in which the upper gastrointestinal tract expels its contents (Hall & Guyton, 2011; Kovac, 2000; Watcha & White, 1992). This often occurs when the upper digestive tract is over distended, irritated, or hyperactive (Hall & Guyton, 2011; Kovac, 2000; Watcha & White, 1992). Vomiting is a complex process in which the body can stop the digestion and further ingestion of gastric contents by expelling them via the oropharynx (Kovac, 2009; Sharkey & Wallace, 2011). Vomiting has three phases: the pre-ejection, ejection, and post-ejection phases (Sharkey & Wallace, 2011; Watcha & White, 1992).

The pre-ejection phase is when antiperistalsis begins, which is movement up the digestive tract (Hall & Guyton, 2011; Watcha & White, 1992). Antiperistalsis is accompanied by salivation, swallowing, pallor, and tachycardia (Hall & Guyton, 2011; Watcha & White, 1992). This phase is then followed by the ejection phase, which consists of retching and vomiting (Watcha & White, 1992). Retching is a contraction of the abdominal and intercostal muscles, along with the rhythmic action of the respiratory muscles against a closed glottis (Sharkey & Wallace, 2011; Watcha & White, 1992). During this phase the hiatal portion of the diaphragm stays contracted, which increases intra-abdominal pressure (Watcha & White, 1992). Ejection of gastric contents occurs when the glottis opens, the esophageal sphincter relaxes, and the rectus abdominis and external oblique muscles contract (Hall & Guyton, 2011; Sharkey & Wallace, 2011; Watcha & White, 1992).

The ejection phase is followed by physiologic responses to return the body back to a calm phase; this can be absent of or accompanied by nausea (Watcha & White, 1992). The complex process of vomiting requires the coordination of several muscles and processes (Watcha & White, 1992). In the post-operative patient, the metabolic expenditure and possible side effects of vomiting place the patient at higher risk for complications. Thus, the high-risk patient must be identified prior to surgery to prevent PONV complications during the recovery phase.

#### PONV Risk Factors

To effectively prevent PONV, high-risk patients must be identified preoperatively. Patients can be at high risk for PONV based on underlying physical disease, the surgical procedure, the duration of anesthesia, or the type of anesthetic administered (Gupta, Wakhloo, Lahori, Mahajjan, & Gupta, 2007; Kovac, 2000; Sinclair, Chung, & Mezie, 1999; Watcha & White, 1992; Wender, 2009). Risk assessment tools are available in identification of patients at high-risk for PONV such as the one developed by Apfel et al. (1998). By using these scoring systems, objective data can be collected to identify potential high-risk patients, which allows for adequate preventative treatment (Hambridge, 2012).

#### *Obesity*

Obesity is considered an increased risk of PONV due to the accumulation of anesthetic gases in the adipose tissue; this accumulation can delay emergence from anesthesia and the return of protective airway reflexes (Hambridge, 2012; Thompson, 1999; Watcha & White, 1992). Due to the obesity epidemic, this can present a problem in preventing PONV. Obese patients can also have larger residual gastric volumes that

place them at a higher risk for PONV (Thompson, 1999; Watcha & White, 1992). Also, obese individuals can present with airway difficulties, which can increase the risk of gastric inflation resulting in higher incidence of PONV (Watcha & White, 1992).

### *Age*

PONV tends to have higher incidences in younger children than that of adults (Gan et al., 2006; Watcha & White, 1992). However, this is contradicted by Thompson (1999), who reported that children were less likely to experience PONV than that of their adult counterparts. Thompson (1999) also states that elderly adults, greater than 55 years old, were less likely to experience PONV for the same operation in a younger individual having the operation. However, the majority of the evidence supports that younger children have a higher incidence of PONV when compared to adults (Gan et al., 2006; Watcha & White, 1992).

### *Gender*

There is a consensus that women have a higher incidence of PONV over that of men (Gan et al., 2006; Hambridge, 2012; Thompson 1999; Watcha & White, 1992). Females are two to three times more likely to experience PONV after puberty, with more severe vomiting (Thompson, 1999). The incidence of PONV increases due to hormonal changes when procedures occur during the menstrual cycle (Watcha & White, 1992).

### *Surgical Procedure and Duration*

Certain surgical procedures also carry higher risk of PONV such as: gynecological, middle ear, laparoscopic surgeries, reproductive, gallbladder, head, neck, and strabismus surgery (Gan et al., 2006, Hambridge, 2012, Thompson, 1999; Watcha & White, 1992). The majority of PONV documented occurred during ovum retrieval



procedures (Watcha & White, 1992). In addition to the type of procedure, the duration of anesthesia also has significant effects on PONV rates (Gan et al., 2006, Hambridge, 2012, Thompson, 1999; Watcha & White, 1992). The patient has increased exposure to emetic agents such as opioids and volatile agent with a longer duration of anesthesia (Gan et al., 2006, Hambridge, 2012, Thompson, 1999; Watcha & White, 1992).

### *Smoking*

Non-smokers are described as having a higher risk of PONV than that of smokers (Gan et al., 2006, Hambridge, 2012, Thompson, 1999; Watcha & White, 1992). In a study conducted by Chimbira & Sweeney (2000), enzyme induction caused by smoking is believed to be the reason that smokers have a lower incidence of PONV. Chimbira & Sweeney (2000) reported that “only 6% of smokers developed PONV compared to 15% of nonsmokers” (p. 540).

### *Additional Factors*

While the above mentioned are the main factors for PONV, there are additional factors that can place a patient at high risk. Some of the additional factors include pain, delay gastric emptying, hypotension, hypovolemia, migraines, and early ambulation after surgery (Gan et al., 2006, Hambridge, 2012, Thompson, 1999; Watcha & White, 1992). All of the factors are additive in determining a patient's risk for PONV.

### *Propofol*

Propofol has been noted to decrease PONV among patients who receive it; however, in the first study to examine the direct antiemetic properties of propofol, Borgeat et al. (1992), demonstrated that in a randomized, double-blind, placebo-controlled study that propofol had significant direct antiemetic properties. In this study,

the placebo that was used was an intra-lipid to help demonstrate and set apart the propofol and its antiemetic properties (Borgeat et al., 1992). This finding was also supported by a double-blinded, randomized comparison of ondansetron and intraoperative propofol to prevent PONV conducted by Gan et al. (1996), which showed that the maintenance of anesthesia with propofol is more efficient in preventing PONV than ondansetron. The studies conducted by Borgeat et al. (1992) and Gan et al. (1996), both support the antiemetic properties of propofol and its use in anesthesia management.

While propofol is known to have antiemetic properties, the site of action is still unknown (Borgeat et al., 1992; Gan et al., 1996; Gan et al., 1997). In a study conducted by Gan et al. (1996) and Gan et al. (1997), it was postulated that the mechanism of action is that of an anti-dopaminergic. Despite the unknown mechanism of action, propofol has been demonstrated to have antiemetic properties (Borgeat et al., 1992; Gan et al., 1996; Gan et al., 1997). There is a significantly decreased incidence of PONV when infused as part of the anesthetic regimen (Borgeat et al., 1992; Gan et al., 1996; Gan et al., 1997).

Once propofol was proven to have antiemetic properties, the next question that developed was how can it be used solely as an antiemetic? Sub-hypnotic doses of propofol were used by Gan et al. (1997) to determine the plasma concentration that was needed to manage efficiently and prevent PONV. Gan et al. (1997) determined that a plasma concentration of 343 ng/ml of propofol was necessary to achieve the antiemetic effects of propofol effectively. This plasma level causes no increase in sedation and can be accomplished by a 10 mg bolus followed by an infusion of 10 ug/kg/min (Gan et al., 1997). This propofol sub-hypnotic dose is supported the previous evidence by Borgeat et

al. (1992), which demonstrated that 10 mg sub-hypnotic doses of propofol, for patients weighing 50-80 kg, demonstrated direct antiemetic effects against PONV.

### Propofol Side Effects

The use of sub-hypnotic doses of propofol is not associated with any increased sedation, cardiovascular changes, respiratory depression, or pruritus (Borgeat et al., 1992; Gan et al., 1997). There is some pain on injection associated with the use of propofol; however, this pain was only slight (Borgeat et al., 1992). Since the administration of the sub-hypnotic dose given to prevent PONV occurs under anesthesia, no pain is experienced by the patient. If the patient is awake when receiving the propofol dose, a study conducted by Picard and Tramer (2000) demonstrated that lidocaine (0.5mg/kg IV) with a rubber tourniquet on the arm 30-120 seconds before the propofol injection can decrease pain of administration. In 60% of the patients, this technique with lidocaine prevented pain with the injection of propofol (Picard & Tramer, 2000). Alternatively, in a study conducted by Scott, Saunders, and Norman (1988), it was found that the most effective technique to prevent pain upon injection was by injecting into a large vein in the antecubital fossa. There was also an acknowledgment that the use of lidocaine also decreased pain upon injection (Scott et al., 1988).

While this small amount of pain upon injection was noted, no other complications were noted with the use of propofol, which places it above other antiemetic medications (Borgeat et al., 1992). Alternative antiemetic medications can cause prolongation of the Q-T interval and cause headaches (Borgeat et al., 1992). Ondansetron or Zofran<sup>TM</sup>, is a 5-hydroxytryptamine (5-HT) antagonist that is similar to serotonin (Bodner & White, 1991; Fowler & Spiess, 2013; Nicholau, 2011; Odom-

Forren, 2014; Sharkey & Wallace, 2011). Ondansetron is a very efficient agent in treating mild to moderate PONV, but does have some Q-T prolongation (Bodner & White, 1991; Fowler & Spiess, 2013; Nicholau, 2011; Odom-Forren, 2014; Sharkey & Wallace, 2011). In a study conducted by Bodner & White (1991), a group of patients that received ondansetron had a 41% lower incidence of PONV than the patient who did not. However, the ondansetron group still had a considerably high number, 43%, of all patients who needed a rescue antiemetic in the recovery room (Bodner & White, 1991).

Ondansetron had been shown to be more efficient when administered with another antiemetic medication, such as dexamethasone (Shora, Gurcoo, Farooqi, Qazi, & Mehrah-ud-Din, (2008). Droperidol, a dopamine antagonist, previously was the choice for antiemetic treatment (Odom-Forren, 2014). However, droperidol has since had a black box placed on it by the Food and Drug Administration (FDA) due to QT prolongation (Odom-Forren, 2014). While the association of Q-T prolongation is with higher dosing regimens, which are much greater than the dose required to prevent PONV; it is still considered more dangerous than ondansetron that can have the same effect on Q-T prolongation (Odom-Forren, 2014). Propofol is a safe alternative or adjunct to prevent these complications.

Since antiemetic drugs have different sites of action, multi-modal treatment can be beneficial to prevent PONV in high-risk patients (Norred, 2003; Watcha & White, 1992). By implementing a multi-modal therapy regimen, lower doses of antiemetic agents can be used due to the additive effects of the different drugs to prevent side effects (Norred, 2003; Watcha & White, 1992). However, care must be taken to avoid the use of multiple drugs with the same site of action to prevent and increased incidence of side

effects (Watcha & White, 1992). Thus, the addition of propofol as an antiemetic could prove very useful in multi-modal treatment for PONV.

One potential complication is a possible reaction with the administration of propofol to a patient with an egg or soy allergy (Murphy, Campbell, & Baines, 2011; Nagelhout, 2014). Propofol contains egg lecithin/phosphatide and soy oil in its lipid suspension (Murphy et al., 2011; Nagelhout, 2014). However, the egg lecithin/phosphatide and soy oil is considered unlikely to cause an allergic reaction (Murphy et al., 2011; Nagelhout, 2014). Besides the proteins from the egg whites that could cause an allergic reaction, the propofol formulation contains heated egg yolk (Murphy et al., 2011; Nagelhout, 2014). While there is no data that supports the avoidance of propofol in egg or soy allergic patients, the consensus differs between countries on whether or not propofol should be administered to these individuals (Murphy et al., 2011; Nagelhout, 2014). Clinicians tend to err on the side of caution and avoid its use in such individuals.

Since propofol is known to have antiemetic properties, many would ask why not use it for all surgical cases? Fombeur et al. (2002) examined the cost comparison and effectiveness of propofol anesthesia versus that of desflurane. While desflurane was cheaper than propofol in providing anesthesia, \$28 versus \$45 respectively, patients in the desflurane group was over five times more likely to experience PONV (Fombeur et al., 2002). Thus, the volatile agent patients would require more nursing time, additional medications, longer PACU times, and have lower patients satisfaction scores (Fombeur, et al., 2002). As healthcare providers, we must carefully examine the risk factors to

ensure that proper use of propofol is used to help improve patient outcomes while also minimizing healthcare costs.

## CHAPTER III

### METHODOLOGY

#### Theoretical and Conceptual Framework

Neuman's system model was the conceptual model for this study. Neuman's system model has two main factors: stress and the systematic feedback loops (Whetsell, Gonzalez, & Moreno-Fergusson, 2011). In Neuman's model, the individual is examined as a holistic being interacting with its environment; however, it is the stress that the individual encounters in its environment can disrupt a person's homeostasis (Martin, 2006). Neuman believed that if the individual's needs were obtained, that the individual would have wellness (Martin, 2006; Whetsell et al., 2011). However, Neuman defined the nurse's role as to assess, manage, and provide interventions at any time that a stressor was identified or perceived (Martin, 2006).

Neuman's conceptual model is very applicable to the anesthesia specialty because of the impact that environmental factors have on patients under anesthesia. As anesthesia providers, an appropriate pre-operative assessment must be completed to develop an appropriate anesthesia plan to transition the patient throughout the perioperative period with as little disturbance by stress as possible. For PONV, by adequately identifying high-risk individuals and implementing a preventative treatment modality, such as sub-hypnotic doses of propofol at extubation, the goal is that the occurrence of PONV will decrease. Based on Neuman's model, the stressor of PONV is the surgery or anesthesia provided along with any factors that would place the patient at high risk for PONV. Advanced practice nurses must have minimal stress for the benefit and wellness of the patients.

The guiding model used for this project was the logic model (Appendix C). The logic model “is a systematic and visual way to present and share your understanding of relationships among the resources you have” (W.K. Kellogg, 1998, p.1). The logic model serves as a conceptual map that guides program development by identifying and utilizing interpersonal and institutional investments (W.K. Kellogg, 1998).

The logic model maps how a program or project should work (W.K. Kellogg, 1998). The logic model can be used to plan effectively, develop, implement, and disseminate results of a project by creating a systematic and logical pattern to follow (W.K. Kellogg, 2014). The logic model visually demonstrates and helps to organize needed activities and the order of events (W.K. Kellogg, 1998). The logic model was used to guide the development and implementation of this project in the clinical setting.

### Setting

The clinical setting for the implementation of this intervention was an obstetrics/gynecologic (ob/gyn) surgical department located in a Level 2 trauma center in Hattiesburg, Mississippi. This specialized surgical department setting provided the ideal environment since the majority of laparoscopic gynecologic surgeries are now being performed in specialty departments that are capable of inpatient and outpatient procedures (Buchh et al., 2009). The ob/gyn surgical department normally provides care for patients that are class I and class II as set forth by the American Society of Anesthesiologists (ASA) (Buchh et al., 2009). This classification of patient status means there are no other diseases present, or the patient has only mild systemic disease, respectively (Sweitzer, 2011). This environment provided an ideal population to implement the proposed evidenced based practice (EBP) intervention. By using propofol



as an antiemetic in sub-hypnotic doses, there was a possibility of PONV prevention with a routinely used drug in anesthesia. Propofol is an excellent choice for gynecologic anesthesia due to a quick recovery of sedation effects with continuance of antiemetic properties for a better outcome, increased patient satisfaction, and faster discharge (Buchh et al., 2009; Ramanathan et al., 2003).

#### Target Outcome

The desired outcome for this identified population was to decrease the incidence of PONV in the immediate post-operative period with minimal side effects. The goal was that PONV rates would decrease due to administering propofol at extubation. This result was measured by evaluating for the incidence of PONV in the propofol intervention group based a verbal analog scale for nausea and physical assessment for vomiting, versus that of the ondansetron only group. Propofol is known to be an agonist for the  $\gamma$ -aminobutyric acid (GABA) receptor, which exerts as an inhibitory neurotransmitter (Nagelhout, 2014; Patel, Patel, & Roth, 2011). While the mechanism of the antiemetic effect is uncertain, propofol is known to have some antiemetic effects (Nagelhout, 2014; Patel, Patel, & Roth, 2011, Ramanatham et al., 2003; White & Eng, 2013). However, in a limited study conducted by Ramanathan et al. (2003), propofol in sub-hypnotic doses grossly reduced the incidence of PONV in a treatment group of 20 women undergoing gynecologic surgery versus that of the control group. This study provided a fundamental basis on for generation of further EBP research.

By using propofol as an antiemetic, there is a possibility to avoid some complications that are associated with other commonly used drugs. One of the best drugs for PONV treatment, droperidol, was labeled with a black box warning by the Food and

Drug Administration (FDA) due to possible fatal QT prolongation which can lead to torsades de pointes arrhythmias (Norred, 2002; Prevention of PONV, 2013). This black box warning by the FDA stopped the routine use of droperidol as an antiemetic due to the risk of possible litigation due to complications (Norred, 2002). However, the medications that replaced droperidol in routine practice, ondansetron and granisetron, also have the adverse side effects of prolongation of the QT interval that is dose dependent (Prevention of PONV, 2013). Another problem with the 5-HT<sub>3</sub> antagonist, ondansetron and granisetron, is that they are best used in practice as a possible prevention of PONV due to the possibility of delay in onset (Prevention of PONV, 2013). Preventative treatment of PONV in all patients is controversial due to the costs that are associated (Prevention of PONV, 2013). These adverse effects are not an issue with propofol, which makes it an ideal antiemetic drug.

### Barriers

There are many obstacles to effective communication and collaboration in the clinical environment that affect the improvement of patient outcomes. One major potential barrier to the collaboration for this clinical project was the regulatory disagreement between the anesthesiologists and nurse anesthetists. While the two professions should be able to collaborate to improve patient outcomes, often physicians want to protect their field and will not support the endeavors of the advanced nursing provider (Chism, 2013). However, the buy-in of the physician in the anesthesia group was a crucial step because often times physicians are associated with the financial accomplishment of the hospital; thus, they are normally a majority of the leadership team and board of directors (Chism, 2013). Hence, without the support of the physicians, there

was little hope of receiving interest from the hospital or gaining approval for implementation. This potential barrier was not an issue for the implementation of this clinical project. There was full support by the physician staff not only of the department of anesthesia, but also of surgery.

The objective was to obtain interest at a hospital to perform the proposed EBP intervention to assess if better outcomes are achieved by decreasing the incidence of PONV in the immediate post-operative period with the use of propofol. The goal was to decrease PONV in the immediate post-operative period that had the possibility of decreasing healthcare costs. By demonstrating a possible improvement in patient outcomes and a reduction in costs; the institution was very amicable in allowing the implementation of the clinical project and possibly support the change of clinical practice if the results supported the intervention.

#### Population

Recruitment of females between the ages of 18-65, undergoing gynecologic, laparoscopic surgery supplied the subjects for this study. A total of 40-50 subjects were the goal, with 20-25 subjects in each group. However, due to limitations and delays of obtaining university research approval, ten subjects (N=10) were recruited with five subjects in each group. Inclusion criteria included: female, gynecologic surgery, laparoscopic surgery, American Society of Anesthesiologist (ASA) physical status (PS) 1 or 2, and no history of PONV. Exclusion criteria included: diabetes, ASA 3 or 4, history of PONV, systolic blood pressure less than 90 mmHg, a known allergy to eggs, sulfites, or soybeans, non-English speaking individuals, hiatal hernia, diagnosed with gastroparesis, pregnant, currently incarcerated, and patients who refuse to sign informed

consent. A convenience sample was obtained at the surgical department. There was a random assignment of patients to one of two groups, which were blinded to the PACU nurses after gaining consent.

In developing the research question, adult female patients undergoing laparoscopic gynecologic procedures were identified as the target population. It has been identified that the female population undergoing gynecologic laparoscopic surgery are at higher PONV risk due to: female gender, laparoscopic surgery, intra-abdominal surgery and post-operative pain (Butterworth et al., 2013; Joshi & Cunningham, 2013). The additive result of each risk factor for PONV in this population places them at an even higher risk for PONV, which means they have a 70% possibility of developing the complication (Deleskey, 2009). It has been reported that gynecologic surgeries carry the highest risk for PONV, with an incidence of 60-83% in this patient population (Ramanathan, Augustus, Thiruvengadam, Sundaram, & Deepalakshmi, 2003).

The ASA PS classification system, developed in 1941, has become a standard in the field of anesthesia. The intent of this classification system is to assess the general physical status of the patient during the preoperative evaluation (Aronson, McAuliffe, & Miller, 2003; Owens, Felts, & Spitznagel, 1978). The design of the system was to standardize patient classification for statistical methods and consistency in hospital records (Owens et al., 1978). This system does not identify surgical or anesthetic risk for the proposed procedure as it is often misused by anesthesia personnel (Aronson et al., 2003). While the system does have some bias and interrater reliability issues, it is still considered the standard classification system in anesthesia (Aronson et al., 2003).

The ASA PS system was used to classify patient status in the preoperative holding area (Table 1). The ASA PS 1 patient is one that is a normal healthy patient, while the PS 2 patient has mild systemic disease that is well controlled and creates no functional deficits (American Society of Anesthesiologist, 2014; Aronson et al., 2003). Since this study will exclude patients with ASA PS 3, 4, and 5, patients who have diseases that result in functional deficits, a constant threat to life, and not expected to live without the procedure will not be included in the study (Owens et al., 1978). This inclusion criterion will limit to the population to healthy subjects with controlled systemic diseases, thus preventing the inclusion of patients with diseases of a significant nature.

Table 1

*American Society of Anesthesiologist Classification System*

Physical Status	Description
ASA PS 1	A normal healthy patient.
ASA PS 2	A patient with a mild systemic disease.
ASA PS 3	A patient with a severe systemic disease.
ASA PS 4	A patient with a severe systemic disease that is a constant threat to life.
ASA PS 5	A morbid patient who is not expected to live without operation.
ASA PS 6	A patient declared brain dead whom organs are being harvested.
E	Emergent

Note. ASA= American Society of Anesthesiologist. PS= Physical Status

The study included patients who had a negative history for PONV. Excluded were patients who had a previous history of PONV as this was an increased risk factor for

subsequent PONV; this high-risk patient category require the use of a multimodal approach to the prevention of PONV (Gan et al., 2006; Hambridge, 2013). By excluding high-risk PONV patients, appropriate care can be given to them while the accuracy of the study could be maintained.

Excluded were patients who had documented allergies to soybeans and eggs, due to the lecithin content of propofol (Murphy, Campbell, Baines, & Mehr, 2011). Lecithin is contained eggs, soybeans, or other vegetables, which are used in propofol as an emulsifying agent (Murphy et al., 2011). While there is no consensus on whether patients allergic to eggs or soybeans are at increased risk with propofol use, and the product label reads differently between countries, practitioners practice cautiously and avoid the agent in this population (Nagelhout, 2013). Patients also allergic to sulfites could have allergic reactions to generic variations of propofol, thus also requiring exclusion from the study (Nagelhout, 2013). While trade name propofol does not contain sulfites, to ensure, the patient received this formulation of propofol would have complicated logistics. By eliminating this population, there would be a limited number of excluded individuals, if any, due to the low incidence of this allergy (Nagelhout, 2013).

Patients who were hypotensive, as defined by a systolic blood pressure less than 90 mmHg, were excluded from this study. There is a dose-dependent hypotensive effect with the use of propofol (Patel, Patel, & Roth, 2011). Propofol could alter the baroreceptor reflex, cause vasodilation, and depress myocardial contraction, which results in hypotension (Patel et al., 2011). Thus, it is advised that propofol be used with extreme caution in patients who are experiencing hypotension (Patel et al., 2011).

Other individuals excluded from the study were those with gastroparesis, diabetes, and hiatal hernia; non-English speaking and those who refuse to sign the consent form. Patients with diabetes could have autonomic neuropathy that can decrease gastric motility and can lead to gastroparesis (Inzucchi & Sherwin, 2012; Watcha & White, 1992). Gastroparesis, autonomic neuropathy with diabetes, and hiatal hernia are at an increased risk of gastric fluid aspiration (Marley, Calabrese, & Thompson, 2013; Watcha & White, 1992). These patient populations were avoided based upon an increased risk of aspiration and vomiting post-operatively due to gastric residual volumes (Marley, Calabrese, & Thompson, 2013). The exclusion of Non-English speaking individuals was due to language barriers and the lack of certainty of complete understanding of the information provided to them.

Finally, anybody who refused to sign a consent form, was pregnant, or currently incarcerated was excluded based on research protocols as set forth by The University of Southern Mississippi and the institutional review board (IRB). Pregnancy and incarcerated individuals are considered highly vulnerable; thus, they were not included in this study. This exclusion ensured that potentially vulnerable individuals remained protected.

### Sampling

A convenience sampling method was employed, at an ob/gyn surgical department in Hattiesburg, Mississippi, to enroll subjects into the pilot study. Convenience sampling can introduce bias into the sample, but is often used in a pilot study to help develop more in-depth protocols for larger studies (Houser, 2008; Grove et al., 2013). Participants were randomly assigned a group after they have enroll in the study, to help control bias in

the sample (Houser, 2008). Data was collected to allow for an adequate description of the sample to identify any possible prejudice (Grove et al., 2013).

Recruitment of the subjects occurred at the surgical center through personal communication. The initial communication is the most important in this type of recruitment; thus, it should be pleasant, culturally sensitive, informative, and nonaggressive (Grove et al., 2013). The communication should regard the subject as a valuable resource for the researcher (Grove et al., 2013). The patient was ensured that if he/she refuses to complete the study, the surgical center staff would still provide high-quality care without the effect of their decision. Should a participant decline to consent to be in the study, its acceptance was elegant, and care was provided unaffected (Grove et al., 2013).

A total of 10 subjects comprised the sample used for this pilot study. Once patients agreed to participate in the study and consent had been signed, there was random assignment of the subject, to either the comparison group or the treatment group through a random lottery selection process generated by a statistical analysis program. If a patient requests for a particular group placement, he/she will be notified that participation can only be by group randomization. If the patient does not agree to the random group assignment, the patient will be informed that he/she will not be able to participate in the study. The attending anesthesiologist and/or nurse anesthetist were the only staff that knew the assignment of the group placement. The pre-operative and PACU nurses were blinded to the group placement to control bias in the scoring of PONV.

Sample attrition was expected to be nonexistent to minimal; since each subject had limited involvement in the study during their one visit at the ambulatory surgical



center. This one-time encounter limited the opportunity for the subject to withdraw from the study. By having this one-time encounter, the patient did not have any follow-ups with the researcher, which can sometimes be problematic and increase attrition rates by subjects not attending the follow-up (Grove et al., 2013). The attrition rate for this study was zero.

### Research Strategies

To explore the research question, does the administration of sub-hypnotic doses of propofol, as an anti-emetic at extubation, affect post-operative nausea and vomiting (PONV) rates during the immediate post-operative period in adult female patients undergoing gynecologic laparoscopic procedures; a randomized, blinded, controlled comparison group study was completed. This study was a pilot study to determine the feasibility and effectiveness of a larger study in the future.

Since there had not been a generation of point estimates, this intervention was to be conducted as a pilot study. Pilot studies are important in the generation of statistically significant randomized control trials because the feasibility and acceptability of the intervention are assessed, while also allowing alteration and improvement before implementation in a randomized control trial (Grove et al., 2013). By generating data through implementation of the pilot study, adequate sample sizes can be determined through power calculation that can ensure that an appropriate number of subjects are used to determine statistical significance (Grove et al., 2013). Since type II errors can result when the sample is inadequate, the pilot study will be used to support further research in this area if feasible; however, the results will not be generalized to the general population

because the population is non-representative and is often not a normal distribution (Grove et al., 2013).

The use of randomized control trials commonly occur when a convenience sample is used instead of randomized obtained sample pool (Grove, Burns, & Gray, 2013). This type of study does have biases because of the convenience sample, but they also have internal validity because the two groups have similar variables that are crucial to the study (Grove et al., 2013). The non-randomized sample does have external validity threats (Grove et al., 2013).

The random assignment to groups used to place subjects blindly in either a group that received only Zofran™ or a group who received Zofran™ and propofol. The groups assignment remained unknown to the pre-operative and PACU nurses, but not to the anesthesia provider. Since a comparison group is being used, the group that received Zofran™ only were used as a control group. However, there were no ethical concerns since Zofran™ is the standard of treatment for PONV prevention; thus no medical treatment will be withheld. Ondansetron is a selective serotonin (5-HT<sub>3</sub>) antagonist that is routinely used in anesthesia and throughout the medical field for nausea and vomiting prevention and treatment.

### Procedures

After obtaining IRB approval at the clinical site, Forrest General Hospital (Appendix D, E, & F) and The University of Southern Mississippi (Appendix G), the study was executed. The initial step in the implementation process was providing education at the clinical site to the anesthesia providers, recovery room nurses, and pre-operative nurses. This education session provided information to the staff about the study

and how the implementation process would follow. This step of obtaining buy-in from the clinical staff was a crucial goal to the success of the implementation phase of the study.

After education of the staff and clinicians about the pilot study, the actual implementation of the intervention was accomplished. Patients, who consented to be in the study, were randomly assigned to either the control group or the treatment group blindly. This process was accomplished by a random lottery, which assigned the patient a specific three character identifier. The creation of these three character identifiers occurred using a random number generator. This random creation of identifiers prevented any potential patterns recognizable by the recovery room nurses assessing PONV in the PACU. Once the patient was assigned an identifier, there was a corresponding envelope placed with the patient's anesthesia documents, and that remained sealed until in the operating room. This envelope contained instructions to the anesthesia provider on what group the patient had been assigned. The principal investigator collected and placed the patient's demographic data on a pre-printed form. This form was used to analyze demographic data which will include: age, particular type of surgical procedure, race, height, weight, body mass index, smoking status and ASA classification (Appendix A). This data will be retained securely as required by the University of Southern Mississippi and Forrest General Hospital IRB regulations. As Forrest General Hospital has a longer requirement for record preservation, all documents will be kept for six years in a locked box in the principal investigator's personal office. The documents will be available upon request by either IRB committee.

The goal was that each group would have 20-25 subjects, which would have undergone random assignment to the group. However, due to limitations of time due to a delay in IRB approval, there were a total of 10 subjects. The subjects were randomly assigned to a group, with five subjects in each group. All subjects in the control group received Zofran™ (Ondansetron) at induction of anesthesia. Zofran™ was administered at a dose of 0.1 mg/kg if less than 40 kg, and 4 mg if the weight was greater than 40 kg (Sharkey & Wallace, 2011). All patients in the treatment group received Zofran™ at the same dose as the control group at induction of anesthesia, and also received 0.25 mg/kg of propofol at emergence with a max dose of 20 mg. Ondansetron is a selective serotonin (5-HT<sub>3</sub>) antagonist that is routinely used in anesthesia and throughout the medical field for nausea and vomiting prevention and treatment. By administering this to all patients, no care was withheld from the subjects.

In a study conducted by Borgeat et al., (1992), 10 mg of propofol was given and determined to be a sub-hypnotic dose. To correctly account for weight, the avoidance of a blanket dose allowed for consideration of a weight-based approach. Thus, by administering 0.25mg/kg of propofol with a max dose of 20mg, appropriate doses could be given per weight. Since the induction dose of propofol for anesthesia is 1-2 mg/kg, the dose of 0.25 mg/kg was well below the dose that would provide complete sedation (Nagelhout, 2014). There is a decreased incidence of PONV with the administration of propofol for total intravenous anesthesia (TIVA) in patients with known history of PONV due to its antiemetic properties. This TIVA approach requires a constant infusion of propofol during the case at high dosage levels of 100-200 mcg/kg/min to maintain general anesthesia. The cost effectiveness of this anesthetic prevents its use in this

manner in all patients. This study examined the use of small doses of propofol at the end (emergence) of surgery, which is less costly.

Propofol was prepared and labeled per protocol that included aseptic technique and placing the time of preparation on the syringe. All propofol syringes were discarded after 6 hours and used for a single patient administration. Should the anesthesia provider have determined that the propofol syringe was contaminated, they were instructed to discard the syringe and prepare a new syringe of propofol. If there were insufficient propofol left for the sub-hypnotic dose administration at the end of the anesthetic, the patient would have been removed from the study and a new vial would have not been charged.

All patients received a minimum 1 liter of normal saline or lactated ringer (LR) solution replacement using the 4-2-1 formula. Pre-operative fluid management has been shown to prevent hypotension by avoiding vasodilation and to decrease the incidence of PONV by maintaining adequate systemic blood pressure (Lambert, Wakim, & Lambert, 2009). In a study conducted by Lambert et al. (2009), a lower incidence of PONV was observed in patients who received adequate and appropriate fluid replacement.

All patients received a standard intravenous induction of anesthesia with the combination of 0.07-0.15 mg/kg Versed™, 1- 2.5 mg/kg Propofol, 1-1.5 mg/kg lidocaine, 2-50 mcg/kg fentanyl, 1-1.5 mg/kg Anectine, and 0.03 mg/kg Zemuron™ (Butterworth et al., 2013). Appropriate doses were used for the induction of anesthesia based upon the patient's body weight, physical assessment, and anesthesia provider's preference.

Maintenance of anesthesia was obtained by using a standardized concentration of a volatile agent and providing or maintaining normocapnic ventilation. Desflurane 6.0%, sevoflurane 2.0 %, and isoflurane 1.2 % were the inhalational anesthetics used to maintain anesthesia (Butterworth et al., 2013). While these levels are the minimum alveolar concentration (MAC) that is required to prevent movement in 50% of individuals to surgical stimulus, these levels were adjusted as necessary based upon the individual patient (Butterworth et al., 2013). For the purpose of this project, the MAC of the volatile agent was maintained at 0.5-1.5% of MAC per the anesthesia provider's discretion.

Maintenance of mean arterial pressure above 60 mmHg occurred during the procedure. Mean arterial pressure is a calculated measurement using the systolic and diastolic blood pressure measurements to determine blood flow to important organs such as the brain and kidneys. Administration of pain medication as needed to maintain comfort and hemodynamic. Muscle relaxation was achieved as required by rocuronium 0.3mg/kg, atracurium 0.2 mg/kg, or vecuronium 0.05 mg/kg for appropriate muscle paralysis as evident by decreased twitches to train of four (Butterworth et al., 2013). The occurrence of fade, a gradual decline in response to nerve stimulation; or a complete loss of one or more of the four twitches elicited when using a nerve stimulator is supportive of a decrease nerve response (Butterworth et al., 2013). This decrease in nerve response in anesthesia is due to blockade by a neuromuscular blocking drug. The administration of these drugs is monitored by the train of four to determine patient's readiness for emergence and ability to support one own breathing (Butterworth et al., 2013).

Once the surgery was completed, the volatile agents were discontinued, and the treatment group received the assigned dose of propofol during emergence. The definition of beginning of emergence for this project was the beginning of surgical closure. Appropriate muscle relaxant reversal was administered after evidence of return of at least one twitch in train of four (Butterworth et al., 2013). Neostigmine 0.04-0.08 mg/kg and glycopyrrolate 0.2 mg/ml of neostigmine were used to reverse muscle relaxants previously administered (Butterworth et al., 2013). Extubation of the patient occurred after the return of all four twitches without fade. Fade is when the train of four ratio between twitches is less than 90% (Butterworth et al., 2013). Fade means the fourth twitch is less than 90% strong as the first twitch. After extubation, the patient was administered oxygen via a face mask.

After transferring the patient to the PACU, care of the patient was transferred to the PACU nurse at the discretion of the anesthesia provider. Evaluation of the patients occurred by the PACU nurses, who were blinded to the group assignments. The institution requires documentation of nausea and vomiting. Thus, data was collected from the computerized charting and documented on the data collection form by the principal investigator. See Appendix B for a scheduled timeline of this process and the initial goals of the study.

For the purpose of this study, the induction of anesthesia was defined as the time the patient receives the first injection of medication until the airway is secured either by using an endotracheal breathing tube or a laryngeal mask airway, which are breathing tube devices. The securement of the airway was measured by end tidal carbon dioxide and equal bilateral breath sounds. Maintenance of anesthesia began at airway securement

and continued until the beginning of emergence. Emergence started at the beginning of surgical closure and continues until the patient was stable in the PACU.



## CHAPTER IV

## ANALYSIS OF DATA

## Sample Demographics

A recruitment of a total of ten (N=10) subjects occurred for this project at the level II trauma center. This sample was comprised completely of the female gender as required in the inclusion criteria. The subjects were between the ages of 26 and 55, with a median of 36.5 (Table 2). Sixty percent (n=6) of the participants were Caucasian, and 40% (n=4) were African American (Figure 1). All of the subjects (N=10) were classified as ASA 2 patients, meaning each had mild systemic disease.

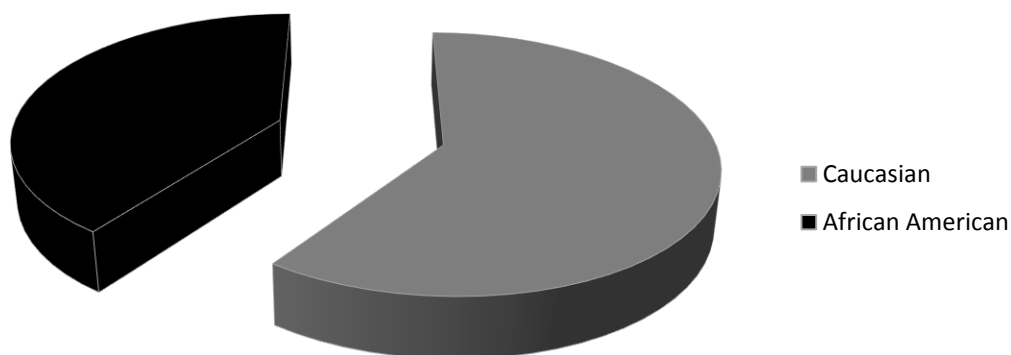
The median height was 65.5 inches with all participants between 63 and 71 inches (Table 2). The weights of the subjects were between 70 and 154 kilograms, with a median of 83.5 (Table 2). By collecting the height and weight of the subjects, the BMI was able to be calculated. The average BMI of the subjects was 33.87, with a minimum of 26.7 and a maximum of 53.4 (Table 2). Ninety percent (n=9) were non-smokers, while 10% (n=1) smoked tobacco.

Table 2

*Sample Demographics*

Total	Item	Mean	Median	Mode	Std.	Minimum	Maximum
N=10	Age	38.8	36.5	26	8.728	26	55
N=10	Height	66.20	65.5	64	2.616	63	71
N=10	BMI	33.87	30.25	30	8.019	26.7	53.4
N=10	Weight	95.8	83.5	70	26.828	70	154

Note. Height is stated in inches. Weight is stated in kilograms.



*Figure 1.* Ethnicity.

#### Procedure Demographics

Data collection of specific procedure information was collected to identify potential effects on PONV incidence. Ninety percent (n=9) of patients had a laparoscopic assisted vaginal hysterectomy (LAVH), with 66.6% (n=6) of those undergoing bilateral salpingo-oophorectomy (BSO). Ten percent (n=1) underwent an exploratory laparoscopic surgery with BSO. The mean anesthesia duration was 113.9 minutes, with a standard deviation of 29.77 minutes (Table 3). The average estimated blood loss (EBL) was 240 milliliters (ml), with a minimum of 50 ml and maximum of 700ml (Table 3). The mean urine output (UOP) was 337.5 ml, with a minimum of zero and maximum of 800 ml (Table 3). The zero could be an error of omission by the anesthesia provider; however, this is unable to be proven and is considered an outlier. The mean amount of fluids administered during anesthesia was 1492 ml with a standard deviation of 424.206 ml (Table 3). This study did not evaluate consideration of the type of fluid administered during surgery.

Table 3

*Procedure Demographics*

Total	Item	Mean	Median	Mode	Standard Deviation	Minimum	Maximum
N=10	Time	113.9	101.5	99	29.377	92	170
N=10	EBL	240	150	150	206.559	50	700
N=10	UOP	337.5	275.0	0	284.129	0	800
N=10	Fluids	1492	1550	700	424.206	700	2200
N=10	PACU Time	57.9	58.5	60	9.303	42	72

Note. Time = minutes. EBL= ml. UOP = ml. Fluids = ml. PACU Time = minutes.

#### Measurement Methodology

PONV severity was self-reported by the patient on a verbal analog scale of 0-10 based on their experience. The use of this assessment technique was a limitation of this study due to the documentation criteria that the clinical facility currently promotes. There was a possibility of some inter-reporter variability between patients due to the differences in experiences and views of the different levels of nausea. Zero on the scale represented no nausea, while ten on the scale represented the worst nausea the patient has ever experienced. Before being discharged from the PACU, patients underwent assessment for nausea. However, if the patient experienced nausea or vomiting, a rescue anti-emetic was provided as ordered by the anesthesia provider. The recovery room nurse documented the patient's nausea score at the time of administration on the electronic medication record.

The null hypothesis for this study was that there is no difference between the means of the control group, who will not receive propofol, and the treatment group, who will receive propofol at extubation. The alternative hypothesis was that there will be a difference between means of the control group and the treatment group. The level of significance that will be used will be 0.05, as this is the maximum level of alpha in scientific research (Houser, 2008).

A t-statistic was calculated from the data, and if lower than the predetermined alpha of 0.05, the null hypothesis will be rejected and the data will be determined as statistically significant (Houser, 2008). The reported result, based on the collected data, includes the test statistic, the p-value, the mean difference between the two groups, and the confidence interval for the average difference. This data will also allow for data points that could be used in further studies to determine adequate sample sizes to determine statistically significant data that would be generalizable.

Rating of vomiting occurred as a yes or no answer by the patient. This vomiting data was used to formulate a chi-square test. The chi-square test allowed the differences in proportion to being determined for vomiting between the two groups. The assumption for the chi-square test is that only one data entry will be collected per patient; this was tracked and compared to the total number of participants.

#### Statistical Analysis

After data collection occurred, a one-tail t-test was performed since only improvement in PONV was being assessed. It is very unlikely that worsening of PONV by propofol since it has been demonstrated to have anti-emetic properties. Also, since there were so many factors of PONV there is difficulty to isolate that propofol was the

culprit. An independent t-test allowed the examination of the differences between the two different groups (Grove et al., 2013). The use of the independent t-test normally involves the assumptions that the sample means from the population are of normal distribution, the dependent or outcome variable is measure at the interval/ration level, the two samples have equal variance, and the observations in each sample are independent (Grove et al., 2013). However, since the t-test is robust, if an assumption has been violated the analysis can still be relied upon (Grove et al., 2013).

The data was entered into Statistical Package for Social Sciences (SPSS) statistical software. A one-tail t-test was performed using a 95% confidence interval. This confidence interval defined the region of scores that is expected to include the true population mean (Aron, Aron, & Coups, 2008). Thus, by setting a 95% confidence interval, there is a 95% chance the populations mean falls within this interval (Aron, Aron, & Coups, 2008).

After calculation of the statistical measurements, there was a noticeable difference in the standard deviations between the control (CX) and treatment (TX) groups (Table 4). The standard deviation of the TX group was 4.472, compared to that of the CX group of zero (Table 4). To analyze the t-test, the Levene's test for equality was used to determine if equal variances should be assumed or not assumed (Table 5).

Table 4

*Group Statistics*

Group	N	Mean	Standard Deviation	Std. Error Mean
TX	5	2.00	4.472	2.000
Nausea Score CX	5	0.00	0.000	0.000

Note. TX= Treatment. CX = Control.

When using Levene's test for equality, the significance ( $p=0.029$ ) is less than the stated level of  $p<0.05$  (Table 5). This determined that equal variances would not be assumed during the analysis of the t-test statistical data. This decision was supported by the differences of standard deviation between the CX and TX groups.

Table 5

*Levene's Test*

		Levene's Test for Equality		t-test for Equality of Means	
		F	Significance	T	Df
Nausea score	Equal variances			1.000	8
	not assumed	7.111	0.029		
	Equal Variances assumed			1.000	4.000

Note. DF = degrees freedom.

To determine if there is significance between the CX and TX means, the significance level between the CX and TX group was examined not assuming equal variances. Since SPSS only calculates a two-tailed t-test, the significance data in the

table was corrected using the calculation to convert the significance level to represent that of a one-tailed t-test. Since the significance level ( $p=0.174$ ) is greater than the alpha level of 0.05, the null hypothesis is not rejected. Thus, a paired samples t-test failed to reveal a statistically reliable difference between the mean of the CX ( $M = 0$ ,  $SD = 0$ ) and TX ( $M = 2.00$ ,  $SD = 4.472$ ) group created during this pilot study,  $t(8) = 1.000$ ,  $p = .0.174$ ,  $\alpha = .05$  (Table 4 & Table 6).

Table 6

*T-Test*

		t-test for Equality of Means				
		Sig.	Mean Difference	Std. Error Difference	95% Confidence interval	
					Lower	Upper
Nausea Score	Equal Variance assumed	0.174	2.000	2.000	-2.612	6.612
	Equal variance not assumed	0.174	2.000	2.000	-3.553	7.553

Note. Sig. = Significance

Table 7

*Case Processing*

		Cases				
		Valid		Missing		Total
Nausea	N	Percent	N	Percent	N	Percent
Score	10	100.0%	0	0.0%	10	100.0%

Data analysis of the vomiting results was accomplished by the generation of a Chi-square analysis in SPSS. A chi-square test was performed and no relationship was found between the CX and TX groups in relation to vomiting,  $\chi^2(1, N = 10) = 1.111, p = 0.146$  (Table 9). To ensure accuracy of the Chi-square analysis, the case processing was analyzed for missing or repeated entries (Table 7). The correct number of data entries were analyzed as evidenced by the total of ten (N=10) entries (Table 7 & Table 8).

Table 8

*Symmetric Test*

		Value	Approx. Sig.
Nominal by	Phi	0.333	0.292
Nominal	Cramer's V	0.333	0.292
Number of Valid Cases		10	



Table 9

*Nausea Score Cross-tabulation*

			Nausea Score		Total
			0	10	
Group	CX	Count	5	0	5
		% within group	100.0%	0.0%	100.0%
		% within nausea score	55.6%	0.0%	50.0%
		% of Total	50.0%	0.0%	50.0%
	TX	Count	4	1	5
		% within group	80.0%	20.0%	100.0%
		% within nausea score	44.4%	100.0%	50.0%
		% of Total	40.0%	10.0%	50.0%
Total		Count	9	1	10
		% within group	90.0%	10.0%	100.0%
		% total	90.0%	10.0%	100.0%

Table 10

*Chi-Square Tests*

	Value	Df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1 sided)
Pearson Chi-Square	1.111	1	0.292		
Continuity Correction	0.000	1	1.000		
Likelihood Ration	1.498	1	0.221		
Fisher				1.000	0.500
S Exact Test					
N of Valid Cases	10				

Since this table is a 2x2, the Phi measure of association will be analyzed instead of Cramer's V (Table 10). The level of association that Phi represents is 0.333 level of association between vomiting and the use of propofol as an anti-emetic.

## CHAPTER V

### SUMMARY

#### Significance and Implications

The results of this pilot study did not show a statistical significance for the administration of the sub-hypnotic doses of propofol in the prevention of PONV. The only patient who experienced PONV in either of the two groups was in the group which received propofol. There were other possible contributing factors that caused the PONV such as the patient received an oral medication prior to the induction of anesthesia. Thus, this could have increased the risk of PONV in this specific patient. The current evidence still supports that propofol as having anti-emetic properties, thus, the limitations of this study must be accounted for, and the study possibly repeated on a more extensive scale.

During a future study, a larger randomized control study could be performed in other patient populations and surgical procedures to obtain a statistically significant outcome. Clinical anesthesia providers attempt to prevent PONV by medications that are available on the market, however, between anesthesia providers there is little consistency and evidence for support of the regimens being administered. If sub-hypnotic propofol proves statistically significant in preventing PONV in the future, the evidence will support the dose and timing of the administration of propofol to prevent PONV.

#### Limitations

There were several limitations encountered during this study. The largest limitation was the lengthy IRB approval process and the limited time frame for the completion of the project. Due to the limited time frame, a small number of subjects were recruited, and the total goal of participants did not occur.

Due to the limited number of subjects used for this pilot study, the results are limited in their use of determining the effectiveness of the intervention. However, the implementation of the intervention allowed the discovery of limitations that need to be accounted for if a larger study was conducted. There needs to be sufficient time for implementation of the study. However, the implementation process would be more efficient if the principal investigator was employed by the hosting facility.

Another limitation encountered was the recruitment of subjects and providers. There was minimal rejection by the patients that were approached, however, the scheduling of the surgeries made the recruitment difficult. The surgeries were scheduled with large lapses of time between the surgeries, making the process inefficient. Also, if the same group of providers could be used the results would be more reliable and consistent due to continuity. All of these are limitations that require consideration in future studies.

#### DNP Essentials

The eight foundational DNP essentials were obtained while implementing this pilot study. Essential I: Scientific underpinning for practice was achieved by performing a complete literature review to formulate an evidenced-based practice plan to decrease PONV by administering sub-hypnotic doses of propofol. This allowed a current practice issue to be addressed using the latest research available. Essential II: Organizational and systems leadership for quality improvement and systems thinking was obtained by collaborating with institutional leadership to provide an intervention to improve quality of care while still considering financial obligations of the institution to provide low cost high quality care. This was accomplished by ensuring that there was no increase in work

on the surgical staff and that there were no increased in costs due to the need of additional pharmaceuticals for the intervention.

Essential III: Clinical scholarship and analytical methods for evidenced-based practice was achieved by performing a literature review of relevant research using electronic databases to formulate the clinical improvement intervention. Clinical scholarship was continued by the writing and copyright of this nursing capstone document which helps to disseminate the findings of this intervention. Essential IV: Information systems/technology and patient care technology for the improvement and transformation of health care was met by using the electronic medical record for data collection. The latest trend in healthcare is to use electronic medical records to improve patient care, however, it allows much quicker and efficient data extraction from medical records than previous paper documents. The data for the project was extracted by the principal investigator from the electronic medical record.

Essential V: Health care policy for advocacy in health care was obtained by influencing committee members and institutional leadership to allow the implementation of the intervention to decrease PONV. During this process, education was able to be provided to these individuals about the role of the advanced practice nurse not only in the clinical realm, but also in improvement of health care outcomes by scholarly activities. Essential VI: Inter-professional collaboration for improving patient and population health outcomes was met by being a leader in the clinical implementation of the clinical intervention. The principal investigator served as the front line leadership with pre-operative and PACU nurses, in addition to the anesthesia providers. The investigator coordinated the care required for participants enrolled in the study. Essential VII:

Clinical prevention and population health for improving the nation's health was achieved by analyzing statistical and scientific data during the needs assessment to determine the need and feasibility of using propofol as a preventative method against PONV. Essential VIII: Advance Practice was obtained by establishing therapeutic relationships with the subjects to improve patient outcomes. This was achieved by developing and implementing the therapeutic intervention.

#### Future Directions

Further research needs to be completed to determine the effectiveness of sub-hypnotic doses of propofol at emergency in preventing PONV. A larger sample cohort needs to be recruited, with a potential for including other high-risk surgical procedure types in the future studies. Future studies should plan ample implementation time and consider using a select group of anesthesia providers to produce consistency in the study. However, the most important part is to disseminate findings of these types of studies. If dissemination is not performed, clinical practice change is unable to be implemented by clinicians to improve patient outcomes on a national and international level.

#### Conclusion

The incidence of PONV remains a concern to practicing anesthesia clinicians. While the statistical data of this pilot study is not overwhelmingly support of the use of propofol as an anti-emetic in sub-hypnotic doses, this pilot study was limited. Further research needs to be continued with this intervention, after addressing the limitations of this study, to determine its potential effectiveness of the use of sub-hypnotic doses of propofol in preventing PONV. The incidence of PONV still requires further research to

determine prevention measures to improve patient outcomes and provide high quality lost cost health care patients to future surgical patients.

APPENDIX A  
DATA COLLECTION FORM

Participant ID #: \_\_\_\_\_ Procedure date: \_\_\_\_\_  
 Age: \_\_\_\_\_  
 Procedure: \_\_\_\_\_  
 Start time: \_\_\_\_\_ End \_\_\_\_\_ Total anesthesia time: \_\_\_\_\_  
 time: \_\_\_\_\_  
 Height: \_\_\_\_\_  
 Weight: \_\_\_\_\_ BMI: \_\_\_\_\_  
 ASA: \_\_\_\_\_

Smoker or Non-Smoker

Caucasian, African American, Hispanic, Other: \_\_\_\_\_

Induction	
Drug	Dose

Maintenance	
Drug	Dose

Emergence	
Drug	Dose

PACU Arrive: \_\_\_\_\_ Discharge: \_\_\_\_\_

Total amount of fluids: \_\_\_\_\_ PONV score: \_\_\_\_\_

EBL: \_\_\_\_\_ UOP: \_\_\_\_\_ Nausea: Yes or No

Rescue Anti-emetic: \_\_\_\_\_



## APPENDIX B

## PROJECTED TIMETABLE

Event	Date
Research proposal approval	September 15, 2014
IRB Submission	September 30, 2014
IRB approval	October 31, 2014
Clinical site education sessions	November 30, 2014
Intervention Implementation	December 1, 2014
Data Collection Completion	May 15, 2015
Rough Draft of final document	July 15, 2015
Oral Defense of Capstone	September 1, 2015
Submit hard copy of project to Graduate reader for proofing	September 2015
Submit final copy to Graduate reader	October 2015

APPENDIX C

LOGIC MODEL

**Logic Model Situation: To decrease PONV in the immediate post-operative period in women undergoing laparoscopic, gynecologic surgeries.**

Inputs	Outputs		Outcomes – Impact		
	Activities	Participation	Short	Medium	Long
<p>Obtain buy in from ambulatory surgical center.</p> <p>Obtain interest from supervising anesthesiologist and operating surgeon.</p> <p>Spark interest in PACU RNs and show benefits of their participation.</p> <p>Develop materials that will help educate patients and develop their desire to participate in the study.</p> <p>Form a collaboration with the pharmacy for propofol syringe preparation.</p>	<p>Conduct information session to educate PACU RNs about PONV instrument rating scale.</p> <p>Develop guideline for pharmacy preparation of sub-hypnotic dose of propofol.</p>	<p>Requires participation of PACU RN and consent from the patient.</p> <p>Requires participation by an ambulatory surgical center.</p>	<p>Decreased PONV rates in the immediate post-operative period.</p> <p>Increased education of the PACU RN about PONV</p>	<p>Faster discharge to stage 2 recovery from stage 1,</p> <p>Quicker oral intake post-operative</p>	<p>Decreased PACU recovery time.</p> <p>Decreased costs for extended PACU stays</p> <p>Increased patient satisfaction scores.</p> <p>Decreased costs associated with PONV complications.</p> <p>Decreased discharge times.</p>
<p><b>Assumptions</b> That there will be enough support through surgery center to implement project</p>	<p><b>External Factors</b> Drug costs Reimbursement</p>				

(W.K. Kellogg, 2014).

APPENDIX D  
FORREST GENERAL IRB APPROVAL



DATE: February 5, 2015

TO: Flem-Flam Aaron Flemister, SRNA, BSN  
FROM: Forrest General Hospital Institutional Review Board

STUDY TITLE: [712956-1] A Pilot Study of Propofol as an Anti-emetic in Laparoscopic, Gynecologic Surgery Patients

SUBMISSION TYPE: New Project

ACTION: APPROVED  
APPROVAL DATE: January 28, 2015  
EXPIRATION DATE: June 30, 2015  
REVIEW TYPE: Full Committee Review

Thank you for your submission of New Project materials for this research study. Forrest General Hospital Institutional Review Board has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Full Committee Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All FDA and sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.

## APPENDIX E

## FORREST GENERAL REVISION APPROVAL



DATE: June 12, 2015

TO: Flem-Flam Aaron Flemister, SRNA, BSN

FROM: Forrest General Hospital Institutional Review Board

STUDY TITLE: [712956-2] A Pilot Study of Propofol as an Anti-emetic in Laparoscopic, Gynecologic Surgery Patients

IRB REFERENCE #:

SUBMISSION TYPE: Amendment/Modification - Revised Informed Consent

ACTION: APPROVED

APPROVAL DATE: June 10, 2015

EXPIRATION DATE: June 30, 2015

REVIEW TYPE: Full Committee Review

Thank you for your submission of Amendment/Modification materials for this research study. Forrest General Hospital Institutional Review Board has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Full Committee Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All FDA and sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

If you have any questions, please contact Michele Stanley at 801-288-4324 or [mstanley@forrestgeneral.com](mailto:mstanley@forrestgeneral.com). Please include your study title and reference number in all correspondence with this office.

## APPENDIX F

## FORREST GENERAL CONTINUE APPROVAL



DATE: June 17, 2015

TO: Flem-Flam Aaron Flemister, SRNA, BSN

FROM: Forrest General Hospital Institutional Review Board

STUDY TITLE: [712956-3] A Pilot Study of Propofol as an Anti-emetic in Laparoscopic, Gynecologic Surgery Patients

SUBMISSION TYPE: Continuing Review/Progress Report

ACTION: APPROVED

APPROVAL DATE: June 17, 2015

EXPIRATION DATE: June 30, 2016

REVIEW TYPE: Full Committee Review

Thank you for your submission of Continuing Review/Progress Report materials for this research study. Forrest General Hospital Institutional Review Board has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Full Committee Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

Please note that any revision to previously approved materials must be approved by this office prior to initiation. Please use the appropriate revision forms for this procedure.

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All FDA and sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

## APPENDIX G

## UNIVERSITY IRB APPROVAL

**INSTITUTIONAL REVIEW BOARD**

118 College Drive #5147 | Hattiesburg, MS 39406-0001

Phone: 601.266.5997 | Fax: 601.266.4377 | [www.usm.edu/research/institutional.review.board](http://www.usm.edu/research/institutional.review.board)**NOTICE OF COMMITTEE ACTION**

The project has been reviewed by The University of Southern Mississippi Institutional Review Board in accordance with Federal Drug Administration regulations (21 CFR 26, 111), Department of Health and Human Services (45 CFR Part 46), and university guidelines to ensure adherence to the following criteria:

- The risks to subjects are minimized.
  - The risks to subjects are reasonable in relation to the anticipated benefits.
  - The selection of subjects is equitable.
  - Informed consent is adequate and appropriately documented.
  - Where appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of the subjects.
  - Where appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of all data.
  - Appropriate additional safeguards have been included to protect vulnerable subjects.
  - Any unanticipated, serious, or continuing problems encountered regarding risks to subjects must be reported immediately, but not later than 10 days following the event. This should be reported to the IRB Office via the "Adverse Effect Report Form".
  - If approved, the maximum period of approval is limited to twelve months.
- Projects that exceed this period must submit an application for renewal or continuation.

PROTOCOL NUMBER: 15020501

PROJECT TITLE: A Pilot Study of Propofol as an Anti-emetic in Laparoscopic, Gynecologic Surgery Patients

PROJECT TYPE: New Project

RESEARCHER(S): Flem-Flam Flemister

COLLEGE/DIVISION: College of Nursing

DEPARTMENT: Advanced Practice

FUNDING AGENCY/SPONSOR: N/A

IRB COMMITTEE ACTION: Full Committee Review Approval

PERIOD OF APPROVAL: 05/14/2015 to 05/13/2016

**Lawrence A. Hosman, Ph.D.**

**Institutional Review Board**

APPENDIX H  
LETTER OF SUPPORT



April 30, 2015

The University of Southern Mississippi  
Institutional Review Board  
118 College Drive #5147  
Hattiesburg, MS 39406

Horace H. Baggett, MD  
Joe H. Campbell, Jr., MD  
C. Hardy Henderson, MD  
Charles A. Henderson, MD  
Luis A. Irizarry, MD  
David Scott Moore, MD  
Timothy W. Norton, MD  
Christopher N. Painter, DO  
David L. Sicard, MD  
William B. Strong, Jr., MD

Dear Institutional Review Board:

This letter is to serve as support for the research that Flem-Flam Aaron Flemister, a University of Southern Mississippi nurse anesthesia student, is proposing for approval. I have talked with him about the proposed capstone project regarding the use of propofol as an anti-emetic in laparoscopic, gynecologic surgery patients and support his efforts in publishing this research.

Propofol is a commonly used drug that is used daily in anesthesia practice. Propofol is known to have anti-emetic properties and is often used in a drug regimen for total intravenous anesthesia in patients at very high-risk for post-operative nausea and vomiting (PONV). Thus, the proposed method of administering propofol at sub-hypnotic doses at the end of the surgical case would only be examining the effect of the timing of the administration of propofol.

In review of the proposed guidelines, patients would continue to receive high quality care that meets all current standards of care and quality measures. All patients would continue to receive preventative care for PONV in the proposed protocol. I believe this proposed project has potential for improving care of patients by decreasing PONV rates and improving patient outcomes.

Sincerely,



Joe Campbell, MD  
Director of Anesthesiology

APPENDIX I  
RESEARCH PROTOCOL

**RESEARCH PROTOCOL**

---

**TITLE:** A Pilot Study of Propofol as an Anti-emetic in laparoscopic, gynecologic surgery patients.

**INVESTIGATORS:** Flem-Flam Flemister, SRNA, BSN

Vickie Stuart, CRNA, DNP

**RESEARCH PLAN**

**A. Clinical Question**

How does the administration of a sub-hypnotic dose of propofol, as an anti-emetic administered during emergence, affect PONV rates in females undergoing gynecologic, laparoscopic surgery?

**B. Background and Significance**

While PONV has been recognized as a common complication of anesthesia for many decades, it remains a major problem of anesthesia practice in the clinical setting today (DeLeskey, 2009; Hambridge, 2012; Thompson, 1999). Among patients that have multiple risk factors, or are considered high-risk patients, PONV incidence can be as high as 70% (Deleskey, 2009; Hambridge, 2012). Abdominal laparoscopic procedures have a higher incidence of PONV due to insufflation of the abdomen and bowel manipulation (Butterworth et al., 2013; Joshi & Cunnigham, 2013; Pawar, Sarkar, & Dewoolkar, 2009). Thus,



laparoscopic gynecologic surgical patients were identified as a high-risk patient population for PONV and the recommendation is that a multimodal antiemetic approach be implemented in this population (Joshi & Cunnigham, 2013).

Propofol has been noted to decrease PONV among patients who receive it. The studies conducted by Borgeat et al. (1992) and Gan et al. (1996), both support the antiemetic properties of propofol and its use in anesthesia management. While propofol is known to have antiemetic properties, the site of action is still unknown (Borgeat et al., 1992; Gan, Ginsberg, Grant, & Glass, 1996; Gan et al., 1997).

### **C.** **Inclusion Criteria**

- Female
- Gynecologic surgery
- Laparoscopic surgery
- No history of PONV
- American Anesthesiologist Association (ASA) Physical Status (PS) 1 or 2
- Age 18-65

### **E.** **Exclusion Criteria**

- Ages less than 18 and greater than 65
- History of PONV
- Diabetes
- Known allergies to soy or egg products
- Systolic blood pressure less than 90 mmHG
- Allergy to sulfites
- Hiatal hernia
- Gastroparesis
- Non-English speaking
- Pregnant
- Currently

### **F.** **Methods**

- Potential candidates for participation will be identified and approached by the principal investigator. Study participation will be explained to patient

and informed consent obtained. Consent will also be obtained from the assigned anesthesia provider to the case.

- Patient will be assigned a unique identifier for the purpose of the study to protect health information. This random identifier will be randomly pre-assigned a designation of control group or intervention group. This information will be provided to the anesthesia provider via a sealed envelope.
- All subjects in the control group will receive Zofran at induction of anesthesia. Zofran will be given at a dose of 0.1 mg/kg if less than 40 kg, and 4 mg if greater than 40 kg (Sharkey & Wallace, 2011). All patients in the treatment group will receive Zofran at the same dose as the control group at induction of anesthesia, and also received 0.25 mg/kg of propofol at emergence with a max dose of 20 mg.
- All patients will receive at minimum 1 liter of normal saline replacement using the 4-2-1 formula.
- All patients will receive a standard intravenous induction of anesthesia with the combination of 0.07-0.15 mg/kg versed, 1- 2.5 mg/kg Propofol, 1-1.5 mg/kg lidocaine, 2-50 mcg/kg fentanyl, 1-1.5 mg/kg Anectine, and 0.03 mg/kg Zemuron (Butterworth et al., 2013). Appropriate doses will be used for the induction of anesthesia based upon the patient's body weight and physical assessment.
- Maintenance will be performed using a standardized concentration of volatile agent and normocapnic ventilation will be provided or maintained. Desflurane 6.0%, Sevoflurane 2.0 %, and Isoflurane 1.2 % will be the inhalational anesthetics used to maintain anesthesia (Butterworth et al., 2013). While these levels are the minimum alveolar concentration (MAC) that is required to prevent movement in 50% of individuals to surgical stimulus, these levels will be adjusted as necessary (Butterworth et al., 2013). Mean arterial pressure will be maintained above 60 mmHg. Pain medication will be provided as needed to maintain comfort and hemodynamic. Muscle relaxation will be used as required by rocuronium 0.3mg/kg, atracurium 0.2 mg/kg, or vecuronium 0.05 mg/kg for appropriate muscle paralysis as evident by decreased twitches to train of four (Butterworth et al., 2013).
- Once the surgery is completed, the volatile agents will be discontinued and the treatment group will receive the assigned dose of propofol immediately before extubation. Appropriate muscle relaxant reversal will be given after evidence of return of at least one twitch in train of four (Butterworth et al., 2013). Neostigmine 0.04-0.08 mg/kg and glycopyrrolate 0.2 mg/ml of neostigmine will be used to reverse muscle relaxants (Butterworth et al., 2013).
- After emergence, the patient will be transported to the PACU by the anesthesia provider. Care will be transferred to the PACU nurse once the anesthesia provider deems appropriate. Patients will be assessed for PONV by the PACU RN, which will be blinded to the group assignments.

Documentation of nausea and vomiting are required by the institution, thus data will be collected from the computerized charting. If a patient in either group experiences PONV, treatment will be provided per the anesthesia provider's post-operative orders. Common post-operative PONV treatment is intravenous ondansetron 0.1mg/kg if less than 40 kg or 4 mg if greater than 40 kg, or Phenergan intravenous 6.25 to 12.5 mg. The PONV data will then be collected from the electronic health record by the primary investigator.

**K. Costs To Subjects:**

There will be no additional costs to the patient because there are often small amounts of propofol left over from induction for use at emergence.

**L. Subject Compensation:**

Subjects and providers will not be compensated for their consent to participate in the study.

**P. References**

Butterworth, J.F., Mackey, D.C., & Wasnick, J.D. (2013). *Morgan & Mikhail's clinical anesthesiology* (5<sup>th</sup> ed.). New York, NY: McGraw-Hill.

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APPENDIX J  
LONG CONSENT FORM



INSTITUTIONAL REVIEW BOARD  
LONG FORM CONSENT

LONG FORM CONSENT PROCEDURES
<p>This completed document must be signed by each consenting research participant</p> <ul style="list-style-type: none"> <li>The Project Information and Research Description sections of this form should be completed by the Principal Investigator before submitting this form for IRB approval.</li> <li>Signed copies of the long form consent should be provided to all participants.</li> </ul> <p style="text-align: right; font-size: small;">Last Edited August 20, 2014</p>

Today's date:	
PROJECT INFORMATION	
Project Title: A Pilot Study of Propofol as an Anti-emetic in Laparoscopic, Gynecologic Surgery Patients	
Principal Investigator: Flem-Flam Flemister	Phone: 601-266-5500
Email: flamm-flam.flemister@eagles.usm.edu	
College: Nursing	Department: Advanced Practice Nursing
RESEARCH DESCRIPTION	
<p><b>1. Purpose:</b></p> <p>I am a doctoral nursing student at The University of Southern Mississippi, supervised by Dr. Vickie Stewart, my faculty advisor. You will be asked to join in a study to confirm and support the use of small amounts of propofol, a medicine commonly used during in anesthesia, to help prevent stomach sickness after anesthesia. Propofol is known to help treat nausea/vomiting and this study will be looking at the usefulness of propofol to prevent nausea/vomiting when given at the end of surgery. This study will allow us to decide if better care can be delivered by using this method. I will not be giving these medicines, and will not be involved in your surgery or anesthesia. Your regular anesthesia provider and surgeon will be involved in your procedure and the regular nursing staff will be giving your care afterwards. There are no extra costs for your involvement.</p> <p><b>2. Description of Study:</b></p> <p>If you agree to join the study, you will be asked to sign this consent form and a release of health information document. A total of 40-50 people will be carefully chosen for this study. Involvement will only be during the surgical procedure and during recovery period from anesthesia. Upon your approval to join, a unique number will be given to you for the duration of the surgical procedure and the time spent in the recovery room. This will make certain your privacy and prevent the use of personal information. You will be assigned to either a group who will receive a routine medication called Ondansetron (Zofran), or a group who will receive Ondansetron (Zofran) and a small dose of an additional drug propofol. This will make sure that you will receive some type of medication to help prevent you from becoming sick after your surgery. Though the medications help prevent feeling sick to your stomach, it cannot be guaranteed that either drug will prevent it from happening completely. If you do feel sick, the health care provider will use more medication or other means to relieve the sickness.</p> <p>Selection of which group you will be in will be performed randomly. This means, like flipping a coin, you will be assigned to one of the groups. There are no special requirements or conditions to be in either group. Your chance of being placed in the study drug (propofol) group is expected at 50%. You cannot choose which group you will be in. If this is not okay, you will not be included in the study. Your anesthesia provider will be aware of your involvement in this study and will provide high quality care. Your anesthesia provider will determine your anesthetic plan based upon their clinical judgment and the standard dosing regimen for each</p>	

drug in which they administer. Every patient will receive an anti-nausea medication at the beginning of their surgery; however, some participants will receive a small amount of extra medication at the end of surgery. Care will be provided in the recovery room following surgery where a nurse will monitor any nausea or vomiting that you experience. If at any time you have nausea and/or vomiting, medication will be provided to you based upon your anesthesia provider's orders.

No care will be withheld for the purpose of this study. The information collected from this study will be studied and reported to Forrest General Hospital at the end, or at any time requested during the carrying out of the study. The results of the study will be published upon completion as a doctoral project at The University of Southern Mississippi. The information and results could also be used to support research and/or review articles that could have the chance of publication in an openly dispersed journal.

### 3. Benefits:

There will be no monetary benefit for involvement in this study. However, your involvement will allow you to support the chance of improving not only your care for this surgical procedure, but the care of future patients. There is a chance that if selected for the intervention group, you could avoid or have a decreased experience of being sick after surgery. This study is receiving no support or money from any sources.

### 4. Risks:

While propofol is a widely used medication, there is a chance of allergic response once the medication has been given to you. This study excludes you if you have a known allergy to soybeans, sulfites, or eggs. AND your anesthesia provider will double check your chart for allergies and other known risk factors. However, there is still a potential for an allergic response. Allergic reactions can be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat or trouble breathing. Propofol is normally used as a medication that induces anesthesia; thus, if a response occurs the study will be stopped and a dose will not be given at the end. If a reaction occurs, your anesthesia team will deliver treatment as needed to ensure your well-being and remove you from the study. Some other side effects of propofol may be a burning pain when it's given to you and a decrease in blood pressure. You will still be asleep when the medication is given to you at the end of surgery and will not feel any burning pain. Also, if at the end of surgery your blood pressure is a lot lower from your normal, the extra medication will not be given and you will be removed from the clinical study.

### 5. Confidentiality:

A unique number will be given to you during your surgical procedure and the time in the recovery room. The unique number will guarantee your privacy by preventing the need to use of any part of your medical record number, name, date of birth, or social security number. Information such as height, weight, ethnicity, surgical procedure, and smoking status will be collected for study. This information will be connected to the unique number, which will be destroyed by method of shredding after six years as required by the hospital. All forms and data will be stored in a locked box in a secure location at the hospital or university.

Your privacy is the utmost importance to the research team, any assumed or actual leak of information will be reported to Forrest General Hospital so that correct action may be taken to protect your privacy. You have the right not to give us this consent, in which case you will not be able to join in this study. If you do not give this permission, your treatment will not be changed or decreased.

### 6. Alternative Procedures:

Your involvement in this study is totally your choice and maybe stopped without reason. If you stop or decide not to join, high-quality care will still be given to you by the anesthesia and surgical staff during your surgical procedure. Should you elect to not join, medications to help keep you from getting sick to your stomach will be given to you based upon the decision of your anesthesia provider. You and/or your health insurance will not be billed extra for the costs of propofol given during the last part of surgery to help prevent nausea if you are selected to receive it in this study. For the usual medical care associated with this surgery, if you have health insurance, the cost of your medical services will be billed to your insurance company. If your insurance does not cover these costs or you do not have insurance, these costs will be your obligation.

## APPENDIX K

## HEALTH INFORMATION RELEASE



INSTITUTIONAL REVIEW BOARD

**AUTHORIZATION TO USE OR DISCLOSE (RELEASE) PROTECTED  
HEALTH INFORMATION IN RESEARCH FORM**

AUTHORIZATION TO USE OR DISCLOSE (RELEASE) PROTECTED HEALTH INFORMATION PROCEDURE	
<p>This form should be used only to obtain permission from research participants to use or disclose their protected health information. It should not be completed for studies that do not involve health information or medical procedures.</p> <ul style="list-style-type: none"> <li>The Project Information section of this form must be completed before submitted for IRB approval.</li> <li>Completed copies of this form must be provided to all research participants before gaining their Authorization.</li> </ul>	
Last edited: March 5 <sup>th</sup> 2014	

Today's date:		Authorization Expiration Date:	
PROJECT INFORMATION			
Project Title: A Pilot Study of Propofol as an Anti-emetic in Laparoscopic, Gynecologic Surgery Patients			Protocol #:
Principal Investigator: Flem-Flam Aaron Femister		Phone: 601-266-5500	Email: flemflam.flemister@eagles.usm.edu
College: Nursing	Department: Advanced Practice	Campus Address: 118 College Dr. #5095 Hattiesburg, MS 39406	
Covered Entity: Forrest General Hospital		<b>Note: The Covered Entity is the organization or institution that will be providing health information of the patient(s), which is protected under HIPAA law, e.g. The University of Southern Mississippi.</b>	
List all individuals at the Covered Entity who will be releasing research participants' health information.			
Information will be collected from the medical record by the researcher.			
Briefly describe the purpose and nature of the research.			
<p>You will be asked to take part in a study to confirm and support the use of small doses of propofol, a commonly used medication during anesthesia, to prevent you becoming sick to your stomach after anesthesia. Propofol is known to help treat nausea/ vomiting and this study will be looking at the usefulness of propofol in preventing you from becoming sick to your stomach when administered at the end of surgery. This study will allow us to decide if better patient care can be provided by using this technique of PONV avoidance.</p>			
Describe the information to be used or disclosed, e.g., all information in the medical record, results of physical examinations, medical history, lab tests, or only health information related to a certain condition.			
<p>A unique number will be given to you during your surgical procedure and the time in the recovery room. The unique number will guarantee your privacy by preventing the need to use of any part of your medical record number, name, date of birth, or social security number. Information such as height, weight, ethnicity, surgical</p>			

procedure, and smoking status will be collected for study. This information will be recognized by the unique number, which will be destroyed by method of shredding after the set time required. Any assumed or actual breach of information will be reported to Forrest General Hospital so that proper action may be applied. Information that will be used will be age, height, weight, body mass index (BMI), ethnicity, surgical procedure, surgical duration, post-anesthesia care unit duration, smoking status, American Society of Anesthesiologist Physical Status, medications administered during the procedure, estimated blood loss, intravenous fluid replacement, and urine output. This information will be used to support results and maybe printed together in research documents or publications.

List all individuals involved in the research who will have access to protected health information.

Principal Investigator: Flem-Flam Aaron Flemister, RN, SRNA, BSN, CCRN  
 Faculty Advisor: Vickie Stuart, CRNA, DNP  
 Statistician: Dr. James Johnson (de-identified data only)

#### PROTECTED HEALTH INFORMATION AUTHORIZATION

The Covered Entity listed above is required by law to protect your health information. If you sign this document, you authorize the Covered Entity to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

If you sign this document, you give permission to the specific individuals listed above at the Covered Entity to use or disclose (release) health information that identifies you to researchers listed above for the indicated research purposes.

This Authorization expires on the expiration date listed at the top of this form.

Please note that you do not have to sign this Authorization. The Covered Entity may not condition (withhold or refuse) treatment or services based on whether you sign this Authorization. Also, if you sign, you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the researchers may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to Principal Investigator using the contact information listed above.

By signing below, I acknowledge that I have read, understood, and approve of the information contained herein and authorize the use of my protected health information in research as designated above.

\_\_\_\_\_  
 Research Participant or Participant Representative

\_\_\_\_\_  
 Date



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