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Granisetron Effectiveness on Postoperative Nausea and Vomiting and the Need for Rescue Antiemetics

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GRANISETRON EFFECTIVENESS ON POSTOPERATIVE NAUSEA AND VOMITING AND THE NEED FOR RESCUE ANTIEMETICS

by

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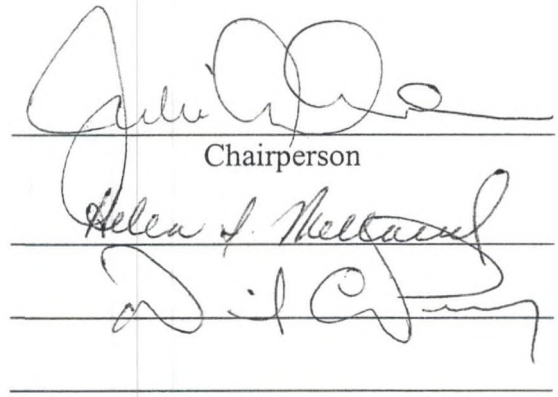

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ABSTRACT

An estimated 20-30% of all surgery patients experience postoperative nausea and vomiting. These percentages could affect more than one million patients every year. The purpose of this study was to look at the effectiveness of low dose granisetron, a common antiemetic used for postoperative nausea and vomiting (PONV). This chart review looked at patients between the ages of 18-70 that had undergone open cholecystectomy and abdominal hysterectomy surgeries at a midwestern rural hospital. This study evaluated those patients that received granisetron and the need for additional antiemetics in the first 24 hours after surgery. This was a retrospective chart review using a convenience sample of 200 patients utilizing a data collection tool designed by the researcher. The study is a descriptive analysis of the use of granisetron for PONV. Data collection was analyzed using Statistical Package for Social Sciences (SPSS) method. The researcher found that a statistically significant number of patients that received low dose granisetron required rescue antiemetics within the first 24 hours after surgery. Of the 200 charts reviewed 179 met study criteria and of these 131 received low dose granisetron during surgery. Of the 131 patients that received granisetron 86 or 65.6% ($p = <.000$) needed rescue antiemetics. Thus, in this patient population low dose granisetron was not effective in decreasing PONV. If PONV is reduced, there will be an increase in patient satisfaction, safety, and a decrease in health care costs. This facility's current protocol for low dose granisetron is not a cost effective intraoperative antiemetic as evidenced by the need for rescue antiemetics in the first 24 hours post-op.

This study did not show a correlation between the use of morphine for post-op pain control and the increased need for rescue antiemetics. The information from this study is beneficial to anesthesia providers in helping prevent and treat postoperative nausea and vomiting and to nursing professionals in helping improve patient outcome and satisfaction following open cholecystectomy and abdominal hysterectomy surgery.

CHAPTER I

INTRODUCTION

While there have been great advances in the field of anesthesia, surgical technology, and pharmacology in the recent years, the incidence of postoperative nausea and vomiting (PONV) continues to be estimated at 20-30% of all surgery patients. This could potentially affect more than one million patients every year in the US. PONV can decrease patient safety and satisfaction and increase patient stress, anxiety, hospital stay, and use of nursing resources. These factors, in turn, can increase health care costs.

Nausea and vomiting affects patients by causing embarrassment and dissatisfaction with the surgical experience. Quellette and Quellette (1998) report that PONV ranks second only to pain on a list of the most feared aspects of surgery. Some patients having surgery stated that "experiencing PONV was more disabling than the operation itself" (Thompson, 1999, p. 1130).

Purpose of the Study

There have been many studies done in the past comparing medication effectiveness on PONV. This study was a retrospective chart review to look at the effectiveness of granisetron (Kytril), a common antiemetic, used for postoperative nausea and vomiting on open cholecystectomy and abdominal hysterectomy surgery in

one 350 bed midwestern rural hospital. This midwestern rural hospital had incorporated granisetron into its standing orders as an antiemetic for both chemotherapy nausea and vomiting and as an antiemetic for nausea and vomiting not related to chemotherapy, which would include PONV (see Appendix A). This study investigated antiemetics given during the intraoperative period, if granisetron was given, the dose, and the need for rescue antiemetics in the following 24 hours postoperative hospital stay.

Significance of the Study

Patient individuality makes PONV more complex, in turn requiring more skillful nursing assessments and knowledge of treatment modalities. According to Rhodes and McDaniel (1999), "managing nausea, vomiting, and retching requires excellent assessment skills, knowledge of pharmacologic actions, and an accurate assessment of the patient's personal symptom experience" (p. 892). Morphine is a common medication used to relieve postoperative pain that has mixed actions. It can depress the vomiting center and decrease pain but it can also slow the gastrointestinal (GI) tract and be a contributing factor in the cause of PONV. This study then looked at the use of morphine for pain control after surgery. Decreasing PONV will increase patient satisfaction and safety, which in turn, will lead to decreased health care costs. The information from this study is beneficial to both anesthesia professionals in helping prevent and treat PONV, and to nursing professionals helping to improve patient outcomes and satisfaction following open cholecystectomy and abdominal hysterectomy surgeries at this midwestern rural hospital.

Research Questions

In considering the use of intraoperative granisetron for non-chemotherapy related nausea and vomiting the research questions for this study were:

1) What is the effectiveness of the current dosing regime of granisetron for the prevention of post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

2) Is there a pattern in the use of rescue antiemetics within the first 24 hours for post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy as evidenced by repeated use of the same rescue antiemetic?

3) Is the current protocol for granisetron a cost effective first line of defense medication as evidenced by no need for rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

4) Is there a relationship between the use of morphine for pain control and the incidence of post-op nausea and vomiting in patients that have undergone open cholecystectomy and abdominal hysterectomy surgery?

Theoretical Framework

The theoretical perspective that guided this study originated from a nursing systems model as proposed by Betty Neuman. Neuman's systems model originated as a holistic way to look at nursing knowledge and was proposed as a teaching tool in 1970 (Gigliotti, 2003). Neuman's systems model relates the living organism as an open system that incorporates all its elements of complex interactions with the organism's environment. The organism may be defined as a patient, client, family, group, or

community. Neuman's systems model is based on the General System theory and also draws upon the Gestalt theory. The "General Systems theory states that all elements in a complex organization are in interaction" (Tomey & Alligood, 2002, p. 300).

The Gestalt theory is based on homeostasis to maintain equilibrium under varying conditions of health. The whole system of the patient interacts with the environment and five variables including, physiology, psychology, socioculture, development, and spirituality. Neuman's model states that an organism must satisfy its needs by using an adjustment process. This adjustment process should be ongoing and dynamic as to satisfy any needs that may disrupt the organism's balance. If this balance is disrupted for extended periods of time illness may occur.

Neuman states that "stress increases the demand for readjustment. This demand is nonspecific; it requires adaptation to a problem, irrespective of the nature of the problem" (Tomey & Alligood, 2002, p. 300). In this model there are both positive and negative stressors that produce tension resulting in a stress response. Neuman has adapted three levels of prevention related to nursing. These three levels of prevention include primary, secondary, and tertiary. Primary prevention refers to decreasing the chance of encountering a stressor. Secondary prevention refers to reducing the effects the stressors has on the organism. This level of prevention may be accomplished through diagnosing the stressor early and effectively treating it. Tertiary prevention attempts to decrease the lasting effects of the stressor after it has been treated.

Neuman states that the organism has lines of resistance to help fight against stressors. These lines of resistance include a normal line of defense and a flexible line of defense. The normal line of defense represents the organism's state of stability and

the flexible line of defense is a dynamic protector. The flexible line of defense prevents stressors from "breaking through the usual wellness state as represented by the normal line of defense" (Tomey & Alligood, 2002, p. 302). Integrity of the organism or system is maintained by adequately coping with the stressors. According to Neuman, Neuman, and Holder (2000), Neuman's systems model "allows for facilitation of nurturing toward stress reduction to offer creative balance and optimal client system stability or wellness. These are logical goals for all healthcare givers" (p. 61).

Having surgery can be classified as a stressor that can cause increased anxiety, tension, and fear. According to Newman's systems model stress increases a demand for adjustment. In the secondary level of prevention stressors can be reduced "through early diagnosis and effective treatment of illness symptoms" (Tomey & Alligood, 2002, p. 301). The purpose of this study reflects early diagnosis and effective treatment of PONV. In decreasing the incidence of PONV the patients will have decreased stress and increased satisfaction to adjust the body back into balance in a timely manner.

Definitions

The major concepts identified and defined for this study are abdominal hysterectomy, antiemetic, granisetron, open cholecystectomy, and PONV.

Abdominal hysterectomy surgery involves surgically opening of the abdominal wall and removal of the uterus and cervix. According to Smeltzer and Bare (1996), hysterectomies are performed for numerous reasons including cancer, uterine bleeding, endometriosis, and prolapsed uterus. This surgery also involves a post-op hospital stay of at least 24 hours.

Antiemetics are defined as any class of medication given in anticipation of relieving or preventing PONV in the first 24 hours post-op.

Granisetron (Kytril) is a serotonin 5HT3 antagonist antiemetic medication used to reduce or eliminate PONV as evidenced by no need for rescue antiemetics in the first 24 hours postoperative after open cholecystectomy and abdominal hysterectomy. According to the standing orders at the study institution the dose of granisetron for adults or pediatric patients is 0.1mg intravenous (IV) intraoperative and every 24 hours as needed.

Open cholecystectomy is a surgical procedure where the abdominal wall is surgically opened and the gallbladder is removed. According to Smeltzer and Bare (1996), "it is one of the most frequent surgical procedures with over 600,00 performed each year" (p. 1011). This surgery requires a post-op hospital stay of at least 24 hours.

Postoperative nausea and vomiting (PONV) is defined as the subjective unpleasant feeling of nausea and the physical act of vomiting within the first 24 hours after open cholecystectomy and abdominal hysterectomy surgery.

Assumptions and Limitations

This study had both assumptions and limitations. Being a retrospective chart review, it was assumed that accuracy of chart data was dependant on personnel documentation in the selected charts. This study also assumes that all medications and information had been recorded accurately. The act of vomiting is not subjective, but individual patient's perceptions of nausea may be subject to patient variability and could be a limitation of this study. Another limitation was that PONV is multifactorial and may not respond similarly to the same antiemetic in each patient. Considering

PONV is multifactorial, it may not be accurately captured by a retrospective chart review. According to Scuderi (2003), "while a variety of potential complications have been attributed to PONV, the exact incidence of most of these complications is unknown"(p.133) and "the actual costs associated with the purported complications of PONV or the additional costs incurred because of admission to hospital secondary to PONV remains extremely difficult to quantify"(p.133). This chart review was limited to charts from one 350 bed midwestern rural hospital, which limits the generalizability of the study.

CHAPTER II

REVIEW OF LITERATURE

This chapter provides a review of the literature that was utilized for this study. Nausea and vomiting mechanisms, treatment modalities, and granisetron were all reviewed from the literature and related to the significance of this study.

Nausea and Vomiting

According to Hansen (1998), nausea is considered a subjective unpleasant feeling. It stems from the stimulation of the vomiting center in the medulla portion of the brain. Hansen defines vomiting as "the sudden, forceful expulsion of the stomach contents" (p. 702). The duodenum is stimulated by sensory receptors from distention of irritation. Signals are then transmitted up to the vomiting center in the brain then back to the alimentary canal affecting the abdominal muscles and the diaphragm. In the lower brain stem or medulla, there is an area known as the emetic center and the triggers for this area stem from the gastrointestinal (GI) tract, inner ear, and the brain itself. Triggers from the GI tract include the presence of bacteria, viral infections, injury, or irritation from chemically sensitive receptors (Davis, 1999).

Vomiting is a stepwise process that follows a specific sequence of events. According to Davis (1999), the sequence of events is as follows: emetic center input, "deep inspiration, opening of the upper esophageal sphincter, closure of the glottis, elevation of the soft palate to close off the internal nares (usually), contraction of the

diaphragm and abdominal muscles, and opening of the lower esophageal sphincter" (p. 2). Following these events the windpipe closes, the abdominal wall muscles and diaphragm tighten forcefully and any food or liquid content in the stomach is expelled. The vomiting center initiates the physical act of vomiting and the chemoreceptor trigger zone (CTZ) is an input area for chemical and humoral substances. The vomiting center is located on the floor of the fourth ventricle of the brain in the medulla oblongata. The central nervous system vomiting center includes areas called postrema, chemoreceptor trigger zone, and the solitary tract nucleus. These are all located by the eighth cranial nerve which controls auditory and vestibular functions, the 4^{th} ventricle, and the cerebellum.

GI stimulation of the vagus nerve is the peripheral mechanism involved with PONV (Kovac, 2003). The CTZ, also located on the floor of the fourth ventricle in the medulla oblongata, responds to chemicals and hormones in the blood and cerebrospinal fluid since it is not protected by the blood brain barrier. The CTZ has receptors for serotonin. The postema has receptors for serotonin, opioid, and dopamine. The solitary tract nucleus has receptors for muscarinic, cholinergic, histamine, and enkephalin. Using a combination of antiemetics should work to block all these receptors in the prevention and treatment of PONV (Kovac, 2003). The CTZ when stimulated releases neurotransmitter impulses that trigger the vomiting center. The vomiting center receives inputs from the CTZ, vestibular system, pharynx, GI tract, vagus nerve, splanchnic nerve, cerebral cortex, hypothalamus, and thalamus and inputs from these areas can all result in the act of vomiting (Davis, 1999). Vomiting occurs when the diaphragm

muscle and abdominal muscles contract and the lower esophageal sphincter opens to allow for expulsion of the contents (Hansen, 1998).

The CTZ is in an area of the brain that is not protected by the blood-brain barrier. Because it is exposed to blood borne substances including toxins, the choice of anesthetic agents is one factor that can be somewhat controlled for in causing PONV (Langer, n.d.). According to Jolley (2000), PONV may affect more than one million patients very year and abdominal or gynecological surgeries were the top two surgeries associated with PONV. Thompson (1999), states that postoperative nausea and vomiting is considered the "big little problem" that is still faced by health care workers today. Although there have been great advances in the field of anesthesia technology and pharmacology the incidence of PONV is estimated at 20-30% of all surgery patients. While these percentages are down considerably from the previous rate of 75% in the ether era, an increased risk of complications accompanies any percent of PONV.

Complications associated with PONV are aspiration, electrolyte imbalances, dehydration, increased hospital stay, increased costs for insurance companies, possible loss of revenue for the hospital, and in severe cases, death. Loss of revenue for the hospital includes factors such as personnel wages, supplies and drugs, increased length of stay, and backup of surgical cases in the operating rooms. In addition, nurses spend multiple hours comforting, assessing, treating, supporting, cleaning up after, and explaining to their patients the mechanisms of nausea and vomiting after surgery (Jolley, 2000; Kovac, 1997; Langer, n.d.; Marley, 1996; Thompson, 1999).

There are many patient related factors that increase the incidence of PONV and they include age, gender, anxiety, obesity, non-smoking history, and prior history of

motion sickness or PONV. An increased incidence of PONV in patients who experience motion sickness and in those that are hypotensive has been reported. Nurses must be aware of all factors that can increase the chance of PONV to anticipate the patient's needs. According to Thompson (1999), preoperative factors such as "age, gender, hormonal balance, weight, gastric contents, prior experience, history of motion sickness, and anxiety" could all contribute to PONV (p. 1132). In adults, women are more likely to have PONV, especially women close to menses in their menstrual cycle. Obese patients may also experience increased levels of PONV. In the obese, the mechanism of PONV has been attributed to the increased time for the body to clear anesthetic agents, due to the anesthetic agents increased affinity for adipose tissue.

The patient groups at highest risk are pediatrics and female in gender, both being associated with a higher incidence of PONV. The mechanisms for decreased PONV in the population that smokes is unknown. Obese patients have a larger drug volume of distribution and fat deposits that affect drug elimination times and can have increased gastric volumes and reflux which all contribute to PONV (Kovac, 2003).

There are also factors that cause PONV associated with all phases of the surgical process. Some of the intraoperative factors that increase PONV are the type of operation, duration, and type of anesthetic used. According to Thompson (1999) laparoscopic, middle ear, ophthalmic, and otolaryngology surgeries all have higher incidence of PONV. Laparoscopic surgeries use carbon dioxide for abdominal distention to increase visualization of the internal organs, this is thought to influence higher rates of PONV. Middle ear and otolaryngology surgeries relate increased incidence of PONV to the swallowing of bloody secretions following surgery. General

anesthesia and a longer surgery time both increase the chance of PONV. This is thought to be related to an increased time the body needs to clear anesthetic agents and an increased time of intestinal immobility. Regional anesthesia techniques are related to a decrease in the risk of PONV (Barash, Cullen, & Stoelting, 2001; Kovac, 2003).

Postoperative factors that increase PONV are pain, hypotension, opioid analgesia, and oral intake. A common cause of PONV is visceral or pelvic pain and "relief of pain was almost always related to relief of nausea" (Thompson, 1999, p. 1132). A common opioid medication used for postoperative pain is morphine and it has mixed effects on controlling pain. According to Thompson (1999) and Bates, Foss, and Murphy (2004), while morphine may depress the vomiting center, it can slow the GI tract causing stimulation of the vestibular nerve that could induce PONV by stimulating the CTZ. Some of the side effects of morphine include respiratory depression, constipation, nausea, and vomiting. In view of this, the use of non-opioid pain medications such as Ketorolac may reduce PONV. Fentanyl is an opioid medication that is currently becoming popular for the relief of postoperative pain. Due to it's chemical properties that differ from morphine it does not produce the same level of side effects as morphine. Fentanyl has a quicker onset of action and shorter duration of action than morphine. Both cause some respiratory depression but fentanyl has a shorter duration, whereas morphine can initiate respiratory depression up to 8-10 hours after its administration. Fentanyl also does not display the nausea and vomiting side effects associated with morphine.

Patients with a history of motion sickness have long been associated with PONV and movement of those patients could potentate PONV. For those patients that also have hypotension the risk of PONV is further increased.

According to Kovac (2003), "to choose when and to whom a prophylactic antiementic should be used, one must consider the patient population and types of surgery that are at high risk for PONV" (p.90). This author proposes categorizing patients into groups of low, moderate, or high risk for PONV. They would be placed in categories based on their individual risk factors and an algorithm would be used to address their potential PONV (Kovac, 2003).

Treatment Modalities

In the treatment of PONV, removal of the irritant or stimulus causing the PONV is the main form of treatment, but this is not always posssible. Another treatment option for PONV is the use of preoperative or intraoperative antiemetic medications. Neuroreceptors in the CTZ have been identified in PONV and different classes of antiemetic medications are designed to block the various receptor sites at the vomiting center to decrease the incidence of nausea and vomiting.

The timing of drug administration is also a consideration and there has been debate as to the best time to give antiemetics. Kovac (2003), stated that antiemetic "administration at the end of surgery is thought to be helpful to prevent PONV because as the stimuli for PONV are increased when the patient emerges from anesthesia". According to Kovac (2000), antiemetics consist of antihistamines, neuroleptics, serotonin 5HT3 antagonists, cannabinoids, and others (see Table 1).

Table 1. Antiemetic Medications

Classes of Antiemetics	*Drug generic name (tradname)*
Antihistamine	Diphenhydramine (Benadryl)
	Dimenhydrinate (Dramamine)
	Hydroxyzine (Vistaril)
	Promethazine (Phenergan)
Neuroleptic (Dopamine receptor blockers)	Prochlorperazine (Compazine)
	Droperidol (Inapsine)
	Chlorpromazine (Thorazine)
	Haloperidol (Haldol)
	Metoclopramide (Reglan)
5HT3 Antagonist	Ondansetron (Zofran)
	Granisetron (Kytril)
	Dolasetron
Cannabinoids	Dronabinol
	Nabilone
Others	Scopolamine
	Corticosteroids
	Benzodiazepines
	Atropine

Antihistamines are medications that block the action of histamines and can reduce the volume of gastric secretions (Barash, Cullen, & Stoelting, 2001). Histamines are produced from amino acids normally present in the body. When they are stimulated their production can increase gastric secretions which can lead to increased nausea. There are two classes of histamines, the H-1 and H-2 receptors (Thomas, 1993). H-1 receptor sites have been identified in the CTZ, so blocking these sites will avoid stimulation of those receptors and histamine production. Antihistamine medications have long been proven effective treatment options for motion sickness and PONV by blocking H-1 and H-2 receptor sites, but they are associated with adverse side effects. These side effects include excessive sedative effects making the patients drowsy. To maximize the benefits of antihistamines they should be administered before surgery.

Neuroleptic medications are drugs that may modify conditions that may be produced by neuroleptic agents such as dopamine (Thomas, 1993). Dopamine receptors have been identified in the CTZ. Neuroleptic or dopamine receptor blockers work by blocking these dopamine receptor sites in the CTZ. Neuroleptic side effects include hypotension, sedation, dystonia, akinesia, and neuroleptic malignant syndrome. While Droperidol has been used for PONV and may be effective for eight hours it is contraindicated in patients with Parkinsonism. In 2001, however the FDA issued what is called a "black box" warning that informed medical persons that droperidol could cause fatal dysrthymias and that alternate medications should be administered. Metoclopromide may be effective in prophylaxis treatment of PONV, it has been shown

to speed up gastric emptying and increase the tone of the gastricesophageal sphincter (Barash, Cullen, & Stoelting, 2001).

The 5HT3 antagonists are medications that may block the serotonin type 3 receptors in the vomiting center, vagal neurons, and the CTZ. The 5HT3 blockers are most effective if given in combination with dexamethasone. Dexamethasone is a corticosteroid medication given in conjunction with these antiemetics to increase their effects. The mechanism by which corticosteroids enhance antiemetic effects is not fully understood. Some of the common side effects related to 5HT3 antagonists are headache, dizziness, diarrhea, and constipation. Dolasetron a 5HT3 blocker has proven very effective in the treatment of chemotherapy induced nausea and vomiting and PONV.

Granisetron, a 5HT3 blocker, was originally developed for use with chemotherapy induced nausea and vomiting and later approved for PONV use. Some studies show the effectiveness of granisetron lasts up to 24 hours. Granisetron, tropisetron, dolasetron, and the newer ramosetron all are effective antiemtics, but none appears to surpass ondansetron for efficacy" (p.1396). According to Barash, Cullen, and Stoelting, (2001), "ondansetron is cost effective if its use shortens post anesthesia care unit (PACU) length of stay, avoids admission, and improves patient satisfaction. Another study by Collis and Hetreed (1994), compared the effectiveness of ondansetron with droperidol and saline on 120 patients undergoing hip and knee replacement surgery. The authors found that patients who received ondansetron did not require a rescue antiemetic as often as those receiving droperidol and saline. Ondansetron proved to be more effective in preventing vomiting than in reducing nausea.

Scopolamine is an antimuscarinic with marked effectiveness on motion sickness, but with atropinic and sedative side effects. As mentioned earlier, other medications used in the treatment of PONV are corticosteroids like dexamethasone, which have been used to increase the effectiveness of some antiemetic medications. Dexamethasone has an adverse side effect of perineal itching and the FDA has not approved this medication for treatment of PONV. It is considered an off label use. Kovac (2003) stated that recent research has shown an improved efficacy of ondansetron or granisetron for PONV from 14 to 24% when given in combination with dexamethasone.

According to McKenzie, Tantisira, Karambelkar, Riley, and Abdelhady (1994), ondansetron used with dexamethasone greatly reduced the incidence of PONV. The study consisted of 180 female patients undergoing major gynecological surgery. In this study group one received ondansetron with saline and group two received ondansetron with dexamethasone. Of the two groups, no emesis or the need for rescue antiemetics occurred in 38% of group one and 52% of group two ($p = 0.048$). McKenzie et al. states "the real benefit to patients will be realized if effective prophylactic combinations of drugs make postoperative nausea and vomiting a rare occurrence" (p. 964). Ultimately, routine use of steroids is not recommended or cost effective and they must be used with caution (Davis, 1999; Langer, n.d.; Thompson, 1999).

There are many other treatments studied in the prevention of PONV. One study of 100 female patients having laparoscopic gynecologic surgery by Winston, Rinehart, Riley, Vacchiano, and Pellegrini (2003), looked at the use of inhaled isopropyl alcohol

compared to ondansetron. The authors stated that "postoperative nausea can be resolved quicker using 70% inhaled isopropyl alcohol compared with intravenous ondansetron" (p. 131). Another study by Ali, Taguchi, Holtmann, and Kurz (2003), researched the use of pre-operative fluids on PONV for 80 patients undergoing laparoscopic cholecystectomy or gynecological surgery. The authors found that patients who received supplemental fluids were less likely to have PONV, stating "supplemental pre-operative fluids is an inexpensive and safe therapy for reducing post-operative nausea and vomiting" (p. 780). Barash, Cullen, and Stoelting, (2001), Kovac (2003), and Scuderi (2003), all stated that hydration may decrease the chance of PONV. There have been multiple studies on alternative treatments that have been researched in the treatment of PONV, like acupuncture, ginger root, and positive suggestion (Langer, n.d.).

Granisetron (Kytril)

Granisetron was approved by the Food and Drug Administration (FDA) for prevention and treatment of PONV on August 19, 2002 (FDA, 2002). Granisetron is one of the serotonin 5HT3 antagonists. It blocks receptors at the vagus nerve site to reduce or eliminate nausea and vomiting, with effects lasting up to 24 hours (Kytril, n.d.). Some of the side effects listed for granisetron are headache, constipation, weakness, drowsiness, and diarrhea. Granisetron was first used in the treatment of chemotherapy induced nausea and vomiting.

According to Fujii, Tanaka, and Kawasaki (2003), "granisetron was significantly more effective than the traditional antiemetics droperidol and metoclopramide for the treatment of PONV" (p. 1149). This study involved 75 female patients undergoing

breast surgery. Three groups were identified; group one received metoclopramide, group two received droperidol, and group three received granisetron. The metoclopramide group reported being 56% ($p = 0.013$) emesis free, the droperidol group reported being 64% ($p = 0.047$) emesis free, and the granisetron group reported being 88% emesis free. This study also found that of the patients who received granisetron and still had nausea, it was less severe. Overall, the researchers showed that patients receiving granisetron had less PONV than their comparison groups.

Fujii, Saitoh, Tanaka, and Toyooka (1998) reported in a study of 120 female patients undergoing laparoscopic cholecystectomy surgery that the minimum effective dose of granisetron is 40 micrograms. According to Gahart and Nazzreno (2005), the proper dosing of granisetron for the prevention and treatment of PONV is 1mg intravenous (IV) given with the induction of anesthesia, before reversal agents are administered, or in the recovery room. Kovac (2003), also recommends 1mg IV for adults at the start or end of surgery. This institution's standing orders dose of granisetron is 0.1mg IV every 24 hours as needed for both adult and pediatric patients. Suboptimal or small doses have been administered when used in combination with another class of antiemetic medication, for example administering granisetron and dexamethasone, a corticosteroid. The small dose of 0.1mg is recommended for pediatric patients, but the larger dose of 1mg is what is recommended for the adult patient.

PONV is multifactorial and there are numerous receptors, as mentioned, that play a role in its causation. Combination therapy has been shown to synergistically improve effectiveness and redosing with the same class of antiemetic or same

medication has not shown to be effective if it did not prove effective with the first dose (Kovac, 2003; Scuderi, 2003). The major draw back of combination therapy is cost. Would all patients need combination therapy or will a single agent surpress PONV in most patients?

Summary of the Review of Literature

PONV continues to be a major complication of surgery. There are many studies on PONV that range from looking at causes to comparing medication effectiveness and alternative therapies. PONV is complex and multifactorial for which continued research is still needed. PONV may be one of the leading causes of hospital admission following elective surgery (Ali et. al., 2003). The literature reviewed supports the use of prophylactic medications, especially in patients with known risk factors, but which medication and how much is very much left to the discression of the healthcare provider and/or doctor.

CHAPTER III

METHODOLOGY

The following chapter discusses the methodology employed in this retrospective chart review of PONV. This descriptive study looked at the effectiveness of granisetron on PONV for patients that have undergone open cholecystectomy and abdominal hysterectomy surgery. This chapter includes discussion relating to the population and sample, study design, data collection methods, instrument reliability and validity, proposed data analysis, and protection of human subjects.

Population and Sample

The population that this study investigated was adult patients ages 18-80 that had undergone open cholecystectomy and abdominal hysterectomy surgeries from an identified regional facility in the midwest. The ICD.9 code used for open cholecystectomy was 51.22 and for abdominal hysterectomy was 68.4. The ICD.9 code is the International Classification of Diseases for use in hospital indexing. This code was developed in 1950 in respond to the need for a basis of storage and retrieval of diagnostic data that would be more efficient. It is a useful tool that is used to classify morbidity data of medical records, ambulatory, medical care programs, medical care review, health statistics, and financial billing. ICD.9 is the ninth revision completed in 1977 (Puckett, 2004).

A convenience sample of 200 patient charts was retrospectively drawn from a 350 bed midwestern rural hospital for chart review. Chart review was completed

by the researcher with a data collection tool designed by the researcher (see Appendix B). Excluded from this study were patients that were unable to verbally communicate the need for antiemetics in the first 24 hours post-op, for example, patients that continue to require mechanical ventilation after surgery.

The sample of open cholecystectomy and abdominal hysterectomy patients was selected based on the information from the literature review. The research by Jolley (2000) related that PONV affects abdominal and gynecological surgeries in the greatest numbers. According to Thompson (1999), adult women experience more PONV than the male population; hence the ICD.9 code for abdominal hysterectomies was selected for this study. Since this population is female, the study attempted to include the male population by selecting the ICD.9 code for open cholecystectomies. Of the 200 charts reviewed, a goal was established to have one quarter of the sample from the male population. In the United States twenty million adults experience gallstones with a higher incidence being female rather than male, of these patients about 600,000 undergo cholecystectomy surgery and the male gender experience more severe symptoms leading to cholecystectomy surgery than females (Gallstones, 1992).

The midwestern rural hospital that was studied adopted protocols for the use of granisetron as a first line medication in the treatment of nausea and vomiting in July 2003. Therefore, this study selected a sample from January 1, 2004 to October 1, 2005. The 200 charts represent 80.9% of the cases for these surgeries during that time frame.

Study Design

This study was a descriptive analysis of the use of granisetron as a first line antiemetic for postoperative nausea and vomiting on patients that have undergone open

cholecystectomy and abdominal hysterectomy surgeries. This study investigated the use of granisetron and the need for rescue antiemetics in the first 24 hours post-op. The researcher investigated the cost effectiveness of granisetron and whether or not morphine was used for post-op pain control. According to Thompson (1999) and Bates, Foss, and Murphy (2004), the use of morphine for pain control may induce PONV.

A retrospective chart review was performed on adult patients ages 18-80 that had undergone open cholecystectomy and abdominal hysterectomy surgery and requiring a post-op hospital stay of at least 24 hours. This study excluded nonverbal patients that were unable to communicate their need for antiemetics. The researcher investigated antiemetics administered during the intraoperative period, if granisetron was administered in the standard dose for this facility and the need for rescue antiemetics in the first 24 hours following surgery.

Variables defined by Gillis and Jackson (2002), are "characteristics of research concepts that are directly measurable and that vary" (p. 716). For this study variables were identified and included age, weight, height, anesthesia type, operative and recovery room minutes, history of prior PONV, ASA Class, recovery room pain score, the use of morphine for intraoperative or postoperative pain control, and antiemetics used. The recovery room pain score used was the highest score verbalized by the patient in a scale of 1-10 with 10 being the worst pain the patient has ever experienced. The goal of this institution is to maintain a pain score of 4 or less; a score of higher than 4 would require the administration of pain medications or initiate contact of the physician for appropriate pain management.

American Society of Anesthesiologiests (ASA) implemented a six category physical status classification system which is utilized to assess a patient prior to surgery. The ASA Class generally correlates with mortality rate during the intraoperative period and is helpful in developing the anesthesia plan for a specific patient. ASA Class range is from 1 to 6 depending on the patients underlying disease processes; an E would denote that the surgery was completed on an emergent basis (Morgan, Mikhail, & Murray, 2002).

Data Collection

A convenience sample of 200 charts was reviewed by the researcher. The self-designed data collection tool included patient demographics consisting of age, height, weight, ASA Class, and gender. According to Thompson (1999), age, gender, and weight can contribute to increased incidence of PONV. The author stated that women may experience increased rates of PONV due to hormonal imbalances via mechanisms not fully understood. The author also related that obese patients may experience increased rates of PONV due to the increased time it takes for the body to clear anesthetic agents, because anesthetic agents have an increased affinity for adipose tissue.

Other information that was obtained through data collection was the type of surgical procedure, history of prior PONV, anesthesia type, operative minutes, recovery room minutes, intraoperative antiemetics administered, the use of morphine for pain control, and antiemetics administered in the recovery room or on the nursing floor within the first 24 hours post-op. According to Thompson (1999), a history of PONV will greatly increase a patient's risk of experiencing PONV again. The author relates

that the longer the surgical time the greater the amount of anesthetic agents administered, which may increase intestinal immobility and the amount of time the body requires clearing the anesthetic agents causing increased PONV. Most patients experience PONV within the first 24 hours post-op, so the researcher concentrated the chart reviews on that time frame.

The ICD.9 codes for open cholecystectomy of 51.22 and abdominal hysterectomy of 68.4 were identified by the coders at this midwestern rural hospital as the codes used for these two specific surgeries. No other modifiers for these ICD.9 codes were identified by the coders.

The patient charges of some antiemetics that were reviewed in this study are as follows: granisetron $28.00 per intravenous dose, metoclopramide $12.50 per intravenous dose, dexamethasone $12.50 per intravenous dose, promethazine $12.50 per intravenous dose, prochlorperazine $18.25 per intravenous dose, and ondansetron $47.50 per intravenous dose. These charges do not include equipment cost and nursing time.

Data Analysis

Data collected was analyzed by the researcher. The Statistical Package for Social Sciences (SPSS) was used in analyzing the data. Frequency distributions and age descriptive statistics were utilized in calculating the patients' demographic information. Data correlations were analyzed using Spearman's nonparametric test and Chi-Square tests. The level of significance was set at $p \leq 0.05$ and the power was set at 0.8 for this study. A power analysis was not deemed necessary to determine the appropriate number of charts to be reviewed for statistical significance.

It was expected that the researcher would find most cases reviewed falling into two groups consisting of the patients that received granisetron during surgery and needed rescue antiemetics during the first 24 hours post-op and the patients that received granisetron during surgery and did not receive rescue antiemetics during the first 24 hours post-op. The majority of the cases reviewed were female aged 18-80 years due to the ICD.9 code for abdominal hysterectomy surgery. The researcher did include the male population by using the ICD.9 code for open cholecystectomy surgery.

Instrument Reliability and Validity

The data collection tool was developed by the researcher. Reliability and validity was accomplished by expert review of the data collection tool. Experts employed in reviewing this collection tool were the researcher's advisor, a certified registered nurse anesthetist, and a medical doctor of anesthesiology. This data collection tool has not been utilized in any previous studies.

Human Subjects

Prior to the start of data collection for this study approval was obtained from the institutional review board (IRB) for this midwestern rural hospital. Patient consent for use of hospital data for research purposes is signed upon admission. These consents were reviewed and if consent was not signed, patient data was not used for this retrospective study. Confidentiality was maintained by limiting access of the data collected. Data collected was kept at the researcher's residence under lock and key. Data will be kept on file for three years and thereafter destroyed. No medical record numbers or patient names were recorded for data collection purposes thus reducing the chance of tracing information back to actual patient's records.

Methodology Summary

This study utilized a retrospective chart review of patients that had undergone open cholecystectomy and abdominal hysterectomy surgeries to explore the effectiveness of the intraoperative dosing regime of granisetron on PONV in the first 24 hours after surgery.

CHAPTER IV

RESULTS

The purpose of this study was to look at the effectiveness of granisetron a common antiemetic used for postoperative nausea and vomiting on open cholecystectomy and abdominal hysterectomy surgery patients. This chapter will cover the characteristic of the sample studied, results from analysis of the research questions, and a summary of the findings for this study. The research questions this study addressed are:

1) What is the effectiveness of the current dosing regime of granisetron for the prevention of post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

2) Is there a pattern in the use of rescue antiemetics within the first 24 hours for post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy as evidenced by repeated use of the same rescue antiemetic?

3) Is the current protocol for granisetron a cost effective first line of defense medication as evidenced by no need for rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

4) Is there a relationship between the use of morphine for pain control and the incidence of post-op nausea and vomiting in patients that have undergone open cholecystectomy and abdominal hysterectomy surgery?

A retrospective chart review was conducted on 200 patients that underwent open cholecystectomy and abdominal hysterectomy surgeries. Of these 200 patients, 179 met the criteria for this study.

Demographics

The researcher reviewed 200 charts and 179 patients met the inclusion and exclusion requirements for this study on postoperative nausea and vomiting after undergoing either open cholecystectomy or abdominal hysterectomy surgery. There were 37 open cholecystectomy patients and 142 abdominal hysterectomy patients, for a total of 179 patients that met study criteria. The open cholecystectomy patients consisted of 23 male patients and 14 female patients and the abdominal hysterectomy patients consisted of 142 females. The mean for patient age was 49.6 years (SD 14.3, range 20 to 80) (see Figure 1). Patient weight had a mean of 86.4 kg (SD 23.2, range 50 to greater than 99) (refer to Figure 2). ASA Classes for this study were mainly Class II (see Figure 3).

Figure 1. The Number of Patients Having Open Cholecystecomy versus Abdominal Hysterectomy By Age Groups

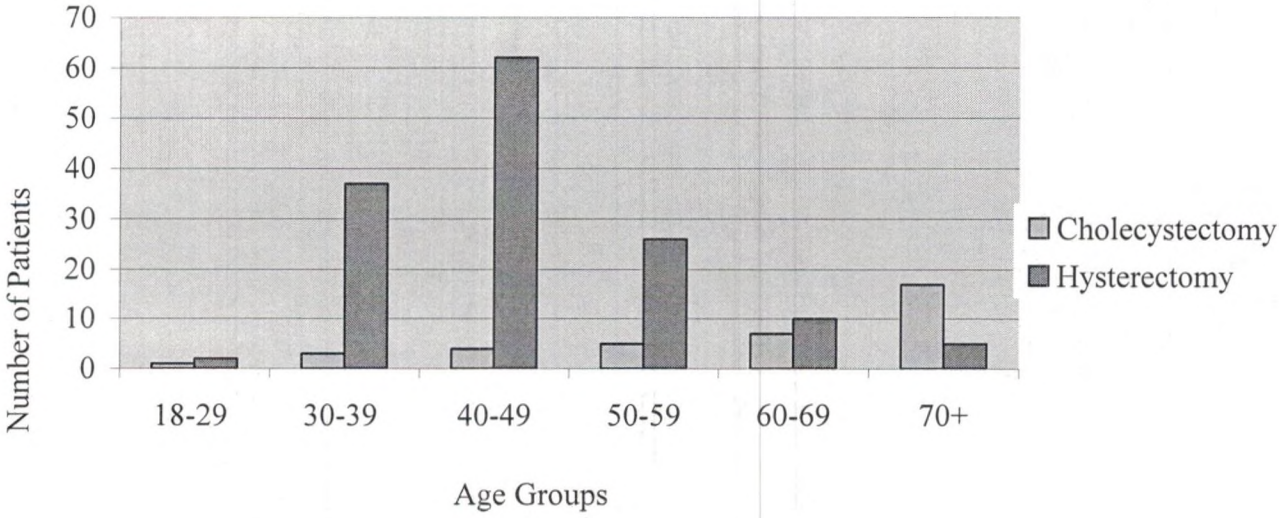


Figure 2. The Number of Patients Having Open Cholecystectomy versus Abdominal Hysterectomy By Weight Groups

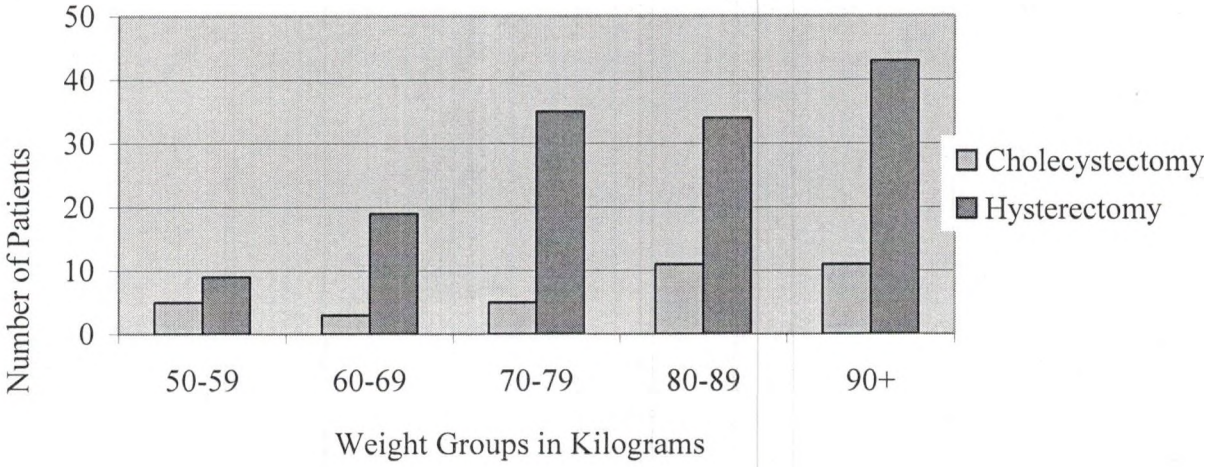
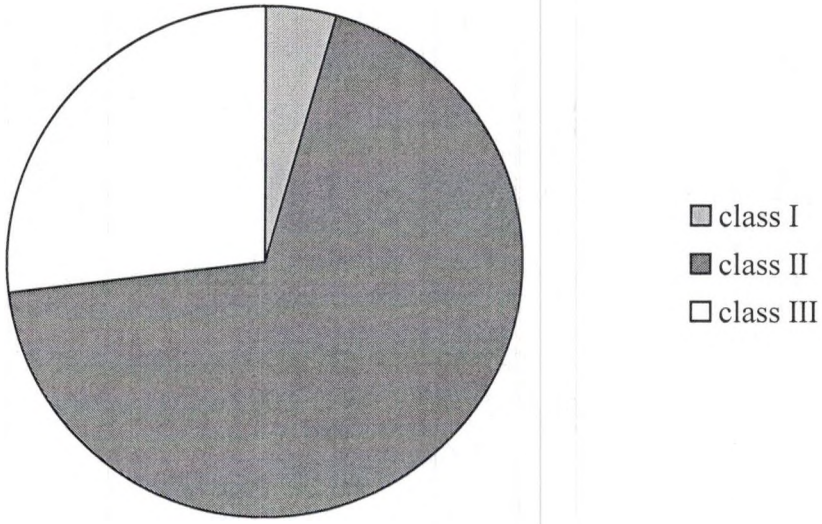


Figure 3. ASA Class For Open Cholecystectomy and Abdominal Hysterectomy Surgical Procedures



Most of the surgeries in this study were performed under general anesthesia and surgical time varied from case to case (see Table 2). Only two (1.4%) of abdominal hysterectomy patients reported having a history of postoperative nausea and vomiting.

No patients having open cholecystectomies reported having a history of postoperative nausea and vomiting.

Table 2. Sample Characteristics

Characteristic	*Open Cholecystectomy*	*Abdominal Hysterectomy*
Number of Patients n=179	37(20.6%)	142(79.3%)
Gender		
Male	23(62.2%)	N/A*
Female	14(37.8%)	142(100%)
Anesthesia type		
General	37(100%)	139(97.9%)
Spinal	0(0.0%)	2(1.4%)
Epidural	0(0.0%)	1(0.7%)
Morphine for RR pain	31(83.8%)	128(90.1%)
OR surgical time		
0-59 minutes	2(5.4%)	22(15.5%)
60-119 minutes	16(43.2%)	94(66.2%)
120-179 minutes	9(24.3%)	22(15.5%)
180-239 minutes	3(8.1%)	2(1.4%)
240-299 minutes	1(2.7%)	0(0.0%)
300-362 minutes	2(5.4%)	1(0.7%)
History of PONV	0(0.0%)	2(1.4%)

*N/A = not applicable

Morphine was used in the recovery room for pain control in 31 (83.8%) of the open cholecystectomy patients and for 128 (90.1%) of the abdominal hysterectomy patients. Pain scores reported from the patients ranged from 1 to 10 with the majority rating their pain in the 4 to 5 range. The 4 to 5 range on the pain scale is considered distracting pain to pain that can not be ignored for more than 30 minutes (see Table 3).

Table 3. Recovery Room Pain Scores

Pain Score	*Open Cholecystectomy*	*Abdominal Hysterectomy*
1-No pain	1	14
2-Mild pain	7	2
3-Annoying pain	3	17
4-Distracting pain	6	6
5-Pain can't be ignore >30mins	6	40
6-Pain can't be ignore at all	2	17
7-Pain making it hard to think	4	10
8-Pain limits activity, nausea	2	11
9-I cry out in severe pain	1	6
10-Worst pain ever, passed out	0	1

Results from Analysis of Research Questions

Data was collected by the researcher in a retrospective chart review of 200 patients undergoing open cholecystectomy and abdominal hysterectomy surgeries, of the 200 charts reviewed, 179 patients met the criteria for this study. Statistical Package for

Social Sciences (SPSS) was used in the analysis of this data. Significance was set at $P \leq 0.05$ for this study.

Research Question 1

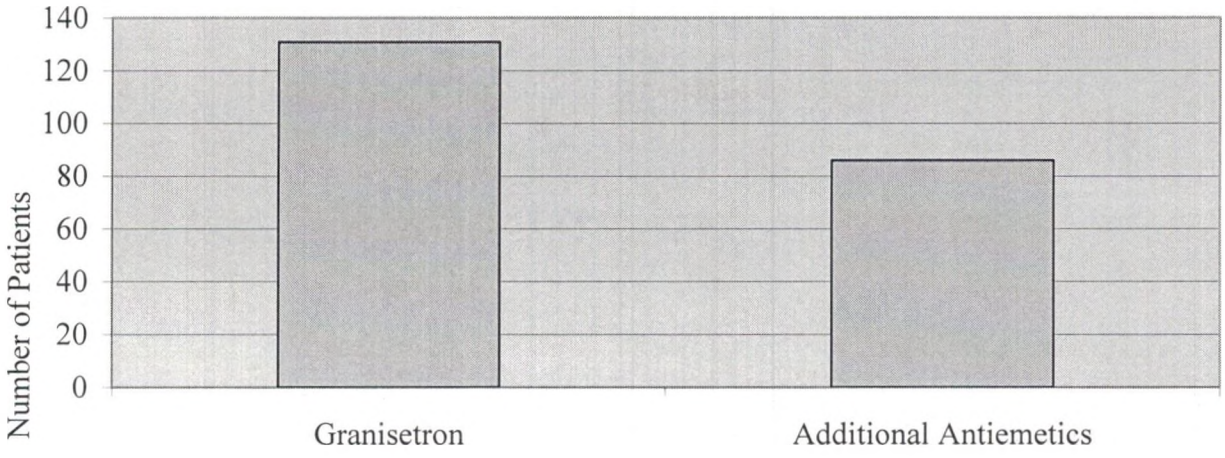
What is the effectiveness of the current dosing regime of granisetron for the prevention of post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

The current dosing regime of granisetron for the study facility is 0.1mg IV every 24 hours. Of the 179 patients that met inclusion criteria, 131 (73.2%) received granisetron 0.1mg IV intraoperatively. Of the 131 patients that received this dosing regime of granisetron 86 (65.6%) also received rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy (see Figure 4). The number of patients receiving rescue antiemetics after this specific dosing regime of granisetron, was statistically significant, Z (observed) 39.23 or $p = <.000$ compared to those patients who did not receive rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy. Of the 86 (65.6%) patients that received rescue antiemetics in the first 24 hours post-op, 31 (36.0%) patients received more than one rescue antiemetic in that 24 hours time frame.

Research Question 2

Is there a pattern in the use of rescue antiemetics within the first 24 hours for post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy as evidenced by repeated use of the same rescue antiemetic?

Figure 4. Patients Receiving Granisetron and Needing Rescue Antiemetics



As reported earlier, of the 131 patients receiving the study dosing regime of granisetron resulted in 86 (65.6%) receiving rescue antiemetics in the first 24 hours post-op. There was a statistically significant number, Z (observed) 39.23 (p = <.000), of patients that required rescue antiemetics, and 31 (36.0%) of those patients required more than one rescue antiemetic to relieve their nausea and vomiting. Of note, most of these patients or 31 (36.0%) required three rescue antiemetics.

A total of 173 rescue antiemetic medications were administered in recovery room and on the nursing floor during the first 24 hours post-op open cholecystectomy and abdominal hysterectomy procedures. The most commonly administered rescue antiemetic was metoclopramide (Reglan), which was administered 98 times and accounted for 56.6% of the rescue antiemetics given. The second most commonly administered rescue antiemetic was promethazine (Phenergan), being administered 36 times and represented 20.8% of the rescue antiemetics given.

Research Question 3

Is the current protocol for granisetron a cost effective first line of defense medication as evidenced by no need for rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

The patient charges for some of the antiemetics reviewed in this study include: (a) granisetron, $28.00 per dose; (b) metoclopramide, $12.50 per dose; (c) prochlorperazine, $18.50 per dose; (d) promethazine, $12.50 per dose; (e) dexamethasone, $12.50 per dose; and (f) ondansetron, $47.50 per dose. These charges do not include nursing time or medical equipment costs, such as syringes to administer the medications. Of the 131 patients that received this dose of granisetron, 86 (65.6%) required rescue antiemetics and 31 (36.0%) of these required three rescue antiemetics to control nausea and vomiting. Considering all these additional charges, this is not a cost effective first line of defense antiemetic for open cholecystectomy and abdominal hysterectomy surgery.

Research Question 4

Is there a relationship between the use of morphine for pain control and the incidence of post-op nausea and vomiting in patients that have undergone open cholecystectomy and abdominal hysterectomy surgery?

Of the 179 patients that met the criteria for this study, 160 (89.3%) received Morphine for post-op pain control in the recovery room. Of the 19 (10.6%) patients that did not receive Morphine for pain control, 7 (36.8%) received rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy procedures. A Chi-Square test of independence or the Spearman's nonparametric correlation two tailed

test comparing the use of morphine for post-op pain and the incidence of post-op nausea and vomiting showed no statistical significance with a $p = 0.704$.

Additional Findings

This study also looked at operating time and patient weight as variables that contribute to PONV after open cholecystectomy and abdominal hysterectomy surgery. This study found no correlation between increased operating time and the increased need for rescue antiemetics in the first 24 hours post-op. A Spearman's nonparametric correlation test showed no significance with a $p = 0.205$. Patients increasing weight groups and the increased need for rescue antiemetics also showed no significance with the Spearman's nonparametric correlation test resulting in a $p = 0.932$.

Result Summary

Most patients in this study were age 40-49 years in the 70-90 kg weight group, and had an ASA class of II. A statistically significant number ($p = <.000$) of patients that received this dosing regime of granisetron required three additional rescue antiemetics in the first 24 hours post-op. The combined additional cost of three rescue antiemetics for 65.6% of the patients exceeded the cost savings of using low-dose granisetron to prevent PONV. Morphine is routinely used in recovery room to treat pain and may contribute to PONV, but 36% of the patients that did not receive morphine still required rescue antiemetics in the first 24 hours post-op.

CHAPTER V

DISCUSSION

The purpose of this study was to look at the effectiveness of low dose granisetron, a common antiemetic. This retrospective chart review investigated 200 charts of patients between the ages of 18-80 that underwent open cholecystectomy and abdominal hysterectomy surgeries during the study period of January 2004 to October 2005. This study investigated antiemetics given during the intraoperative period, if granisetron was given, the dose, and the need for rescue antiemetics in the following 24 hours postoperative hospital stay.

Discussion of Research Questions

This facility's current standing orders and dosing regime of granisetron for post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy does not appear to be effective.

Research Question 1

The first research question for this study was: What is the effectiveness of the current dosing regime of granisetron for the prevention of post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

The 0.1mg IV dose of granisetron intraoperatively required rescue antiemetics in 86 (65.6%) of the 131 patients that the medication, with most patients requiring three rescue antiemetics. This represents a statistically significant number of patients that remained nauseated and/or vomiting 24 hours after surgery ($p = <.000$). Research

studies are consistent with the conclusion that PONV continues to be a main concern for patients and health care providers. PONV can decrease patient safety and satisfaction and increase patient stress, anxiety, hospital stay, and use of nursing resources. These factors, in turn, can increase health care costs. Quellette and Quellette (1998) reported that PONV ranks second only to pain on a list of the most feared aspects of surgery. Some patients having surgery state that "experiencing PONV was more disabling than the operation itself" (Thompson, 1999, p. 1130).

For open cholecystectomy and abdominal hysterectomy surgery, the facility's current dosing of granisetron is not effective as over half the patients experienced PONV after surgery. This facility may need to re-evaluate their standing orders in terms of the current low dose of granisetron being administered. They should consider either trialing a higher dose of granisetron for the adult patients or a different antiemetic from the 5HT3 antagonist class of drugs. The manufactures recommended dose of granisetron for the adult patient is 1mg IV, as listed on the drug package insert. Another 5HT3 antagonist drug would be ondansetron 4mg IV for the adult patient. According to Barash, Cullen, and Stoelting, (2001), "ondansetron is cost effective if its use shortens post anesthesia care unit (PACU) length of stay, avoids admission, and improves patient satisfaction. Granisetron, tropisetron, dolasetron, and the newer ramosetron all are effective antiemtics, but none appears to surpass ondansetron for efficacy" (p. 1396). Another study by Collis and Hetreed (1994) compared the effectiveness of ondansetron with droperidol and saline on 120 patients undergoing hip and knee replacement surgery. The authors found that patients who received ondansetron did not require a rescue antiemetic as often as those receiving droperidol

and saline. Ondansetron proved to be more effective in preventing vomiting than in reducing nausea.

The high number of patients having PONV after surgery could reflect poorly on this facility's patient satisfaction rating. In order to prevent a poor rating, this facility needs to improve on the occurrence of PONV after surgery for open cholecystectomy and abdominal hysterectomy. Patients are more health conscious than ever and with the rising costs of health care; consumers want quality health care at affordable prices. Patients now assess and compare facilties and make their own decision on where they choose to be a patient.

This researcher saw first hand that the 0.1mg dose of granisetron was not effective. Witnessing patients having continued nausea and vomiting after this medication was administered is what prompted this study. The high percent of patients that continued to have PONV in this study was significant and could easily lead to adverse patient effects including increased dissatisfaction, stress, anxiety, and decreased patient safety following surgery.

Research Question 2

The second research question for this study was: Is there a pattern in the use of rescue antiemetics within the first 24 hours for post-op nausea and vomiting in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy as evidenced by repeated use of the same rescue antiemetic?

In this study, a consistent pattern in the consistant use of rescue antiemetics within the first 24 hours post-op following open cholecystectomy and abdominal hysterectomy surgeries was noted. A total of 173 rescue antiemetics doses were

administered during the first 24 hours after surgery. The most commonly used rescue antiemetic was metoclorpramide (Reglan). Metoclorpramide was administered 98 times and accounted for 56.6% of the rescue antiemetics administered. It was followed by Promethazine, which was administered 36 times accounting for 20.8% of the rescue antiemetics. These figures represent a large amount of rescue antiemetics being given to patients that received granisetron during surgery. This consistent pattern of rescue antiemetic use emphasizes that the current dose granisetron is not adequate and thus not effective for this population of patients.

Research Question 3

The third research question for this study was: Is the current protocol for granisetron a cost effective first line of defense medication as evidenced by no need for rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal hysterectomy?

Granisetron does not appear to be cost effective as a first line antiemetic at the current dosing level as evidenced by the continuous need for rescue antiemetics in the first 24 hours after open cholecystectomy and abdominal hysterectomy surgery. Patients consistently needed rescue antiemetics, with most patients requiring three additional medications. The most commonly used rescue antiemetics were metoclopramide at $12.50 per dose, then promethazine at $12.50 per dose, followed by dexamethasone at $12.50 patient charge per dose. Most patients received three additional antiemetics. Thus, they received $37.50 in medication charges for antiemetics along with the charge for granisetron, which is $28.00 per patient dose. Out of 131 patients that received granisetron 86 received rescue antiemetics again with most

receiving three additional medications this would be an additional cost of $3225.00 (86 patients X $37.50). This figure does not including the cost of granisetron. These numbers represent just these two types of surgeries: open cholecystectomy and abdominal hysterectomy. If this study found this great of a need for rescue antiemetics with just these two surgeries, it would make sense then that there is an increased need for rescue antiemetics with other surgeries at this specific facility as well.

Research Question 4

The fourth research question for this study was; Is there a relationship between the use of morphine for pain control and the incidence of post-op nausea and vomiting in patients that have undergone open cholecystectomy and abdominal hysterectomy?

The relationship between morphine administration for pain and the increased incidence of PONV has been well documented by previous studies. A common cause of PONV is visceral or pelvic pain and "relief of pain was almost always related to relief of nausea" (Thompson, 1999, p. 1132). Morphine is an opioid that is frequently used postoperative for pain management with mixed effects. According to Thompson (1999) and Bates, Foss, and Murphy (2004), while morphine may depress the vomiting center, it can also slow the GI tract causing stimulation of the vestibular nerve, thereby inducing PONV through stimulation of the CTZ.

This study showed that 36% of the patients who did not receive morphine still had PONV and required additional antiemetics. Although there were only a small number of patients that did not receive morphine, less than half of those patients required additional antiemetics. The chi-square test of independence, comparing the use of morphine for post-op pain control and the incidence of nausea and vomiting

using the history information was not significant. It is hard to differentiate what is causing the PONV: the surgery, the medications used during, or the medications used after especially the use of morphine for pain relief. This researcher does not know why this study did not show a correlation between the use of morphine for pain control and an increased need for nausea and vomiting medications. Perhaps morphine is so commonly used that health care providers need to consider it routine and account for morphine when considering what antiemetics will best treat PONV. The low dose granisetron used at this facility may have masked the nausea attributed to the use of morphine because the need for rescue antiemetics was so great.

Additional Findings

Obese patients and surgery expected to have longer duration time may require additional antiemetics or multimodal therapy to help prevent PONV for this population of patients. Obese patients have a larger drug volume of distribution due to increased fat deposits that affect drug elimination times and can have increased gastric volumes and reflux which all contribute to PONV (Kovac, 2003). The type of anesthesia administered and longer surgery times both increase the chance of PONV (Barash, Cullen, & Stoelting, 2001; Kovac, 2003). This is thought to be related to an increased time the body needs to clear anesthetic agents and an increased time of intestinal immobility.

This study did not find any correlation between body weight and surgery time to an increased need for antiemetics. The consistent use of rescue antiemetics was seen in all weight groups and in all surgical time groups. The high incidence of PONV in this study may be mostly related to the type of antiemetic used or the low dose granisetron.

For almost all other classes of medications administered there is an adjustment for weight or age group. For example, pediatric patients on average receive smaller doses of medications than adult patients. This facility gives a pediatric patient that may weigh 10 pounds the same low dose granisetron as an adult patient that may weigh 200 pounds. This volume of distribution for granisetron doesn't appear justified. Normally, at home parents give their children smaller doses of Tylenol than they themselves would take. This should hold true for all antiemetics also. Ondansetron (Zofran), has a larger recommended adult dose than pediatric dose, and this is the same class of antiemetic as granisetron, that is a 5HT3. This study found that the dose of granisetron used by this facility is not effective as evidenced by the consistent need for rescue antiemetics in the first 24 hours after surgery.

Implications for Nursing

This study is of significant benefit to all health care providers, including anesthesia providers, nursing staff, nursing educators, pharmacy providers, administration or policy development, and quality improvement staff. According to Rhodes and McDaniel (1999), "managing nausea, vomiting, and retching requires excellent assessment skills, knowledge of pharmacologic actions, and an accurate assessment of the patient's personal symptom experience" (p. 892). The more evidence based research practice health care providers base their own practice on the better patient care and increased patient satisfaction health care facilities will experience.

Implications for Practice

Anesthesia providers can adjust their patient plan of care according to the results of this study. They may continue to use this low dose granisetron knowing the results

of this study or choose a different antiemetic in this class of drugs. Another option would be to routinely administer additional antiemetics in anticipation of the need for rescue antiemetics. Anesthesia providers will benefit in being able to better help prevent and treat PONV. The nursing staff will also benefit from this study as they will be able to help improve patient outcome and satisfaction by anticipating the need for additional rescue antiemetics if granisetron was used. Nurses will be able to choose antiemetics that they have found to work better for this patient population. Improved management of PONV will increase patient satisfaction, decrease costs, decrease nursing time costs, and increase patient safety.

In addition, nurses spend multiple hours comforting, assessing, treating, supporting, cleaning up after, and explaining to their patients the mechanisms of nausea and vomiting after surgery (Jolley, 2000; Kovac, 1997; Langer, n.d.; Marley, 1996; Thompson, 1999). The quality improvement staff could track patient satisfaction or dissatisfaction with the current granisetron dosing regime, or they could help design a study to trial a different antiemetic or different dose of granisetron for this facility. Improvements on the management of PONV following granisetron use would then provide evidence based decisions.

Implications for Education

The nursing educators can benefit from this study by helping educate new nurses on evidence based practice of what works and what has been shown not to be effective. Educators can also use this imformation in helping students be able to anticipate their patients' needs. Educators in the CRNA programs can also use this information for evidence based decision making in teaching students about how to treat PONV.

Implications for Policy

Administration and the staff that change or revise policies can benefit from this study. The results of this study could help administrators make more informed decisions on the policies that help improve patient satisfaction, decrease patient costs, decrease patient anxiety and stress, decrease hospital stay, decrease use of nursing resources, and decrease health care costs to the facility. Specifically, they can make informed decisions on what medication may not be as cost effective as they originally thought. They may also choose to trial a different antiemetic or trial a higher dose of granisetron.

Evidence based decision making for this facility could decrease health care costs to both the patient and the facility. Complications associated with PONV are aspiration, electrolyte imbalances, dehydration, increased hospital stay, increased costs for insurance companies, possible loss of revenue for the hospital, and in severe cases even death. Loss of revenue for the hospital includes factors such as personnel wages, supplies and drugs, increased length of stay, and backup of surgical cases in the operating rooms.

Implications for Research

This study can enhance evidence-based nursing practice and decision making. Further research could be conducted on the effectiveness of administering a higher dose of granisetron. Additional comparison studies could trial the effectiveness of a different 5HT3 antagonist class of medication. PONV has been studied in the past and continues to be investigated as newer and more effective medications continue to be developed, trialed and approved for use.

Results in Terms of Neuman's Model

Neuman's systems model relates the living organism as an open system that incorporates all its elements of complex interactions with the organism's environment. Neuman states that:

> Stress increases the demand for readjustment. Neuman has adapted three levels of prevention related to nursing. These levels of prevention include primary, secondary, and tertiary. Primary prevention refers to decreasing the chance of encountering a stressor. Neuman's systems model allows for facilitation of nurturing toward stress reduction of offer creative balance and optimal client system stability or wellness. These are logical goals for all healthcare givers. (p. 61)

The purpose of this study reflects early diagnosis, effective treatment, and primary prevention of PONV. In decreasing the incidence of PONV, patients can have decreased stress and increased satisfaction to adjust the body back into balance in a timely manner.

The actions and decisions of the healthcare providers can facilitate smooth interactions with the patient and a better understanding of the stress the patient encountered from the surgical experience. The more satisfying or less stressful the patient's surgical experience is the faster the body will return to optimal wellness or stability.

Conclusion

The facility in this study had a significant number of patients needing rescue antiemetics in the first 24 hours post-op open cholecystectomy and abdominal

hysterectomy surgeries after receiving low dose granisetron. However, as stated previously, PONV is multifactorial and each patient has their own perceptions of nausea and unique way of reacting to medications that are administered for PONV. Patient individuality makes PONV complex, in turn, requiring more skillful nursing assessments and knowledge of treatment modalities. According to Rhodes and McDaniel (1999), "managing nausea, vomiting, and retching requires excellent assessment skills, knowledge of pharmacologic actions, and an accurate assessment of the patient's personal symptom experience" (p. 892). The facility in this study should evaluate their current standing orders and dosing of granisetron to decrease the number of patients experiencing PONV. Decreasing PONV will lead to increase patient satisfaction and decrease health care costs for this facility.

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Appendix A

Granisetron Standing Orders

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Granisetron Standing Orders

STANDING ORDERS - ANTIEMETICS FOR NAUSEA & VOMITING NOT RELATED TO CHEMOTHERAPY — PAGE 1 OF 1

1. [ ] Granisetron (Kytril®) 0.1mg IV every 24 hours as needed.*

*If Granisetron (Kytril®) has been given (during surgery, procedure, etc.)—proceed with a different agent for control of nausea and vomiting, do not re-dose the Granisetron.

2. **ADULTS** - For breakthrough nausea and vomiting: (Check additional agents as needed)

[ ] Dexamethasone 4-8mg IV every 24 hours as needed (maximum of two doses)

[ ] Metoclopramide 10mg IV every 4-6 hours as needed

[ ] Promethazine 12.5-25mg IV/IM every 4-6 hours as needed

[ ] Prochlorperazine 5-10mg IV/IM every six hours as needed (**if available**)

3. **PEDIATRIC** – For breakthrough nausea and vomiting: (Check additional agents as needed)

[ ] Granisetron (Kytril®) 0.1 mg IV every 24 hours as needed.

[ ] Dexamethasone 0.2 mg/kg/day IV every 24 hours as needed. (Maximum dose of 8 mg /24 hours.)

[ ] Metoclopramide 0.2 mg/kg/dose IV every 6 hours as needed. (Maximum total of 0.8 mg/kg/day.)

[ ] Promethazine 0.25-1 mg/kg/dose IV/IM every 4-6 hours as needed with a maximum of 25 mg per dose.

[ ] Prochlorperazine 0.1 mg/kg/dose IM every 6-8 hours as needed with a maximum dose limit of 40 mg per day, (**if available**).

A different agent from the above list should be added until nausea and vomiting are controlled. e.g. If Granisetron (Kytril) was given in surgery, give Dexamethasone; if nausea continues proceed to metoclopramide, following Altru Health System Policy/Protocol for nausea and vomiting not related to chemotherapy.

Signature:_____
DATE/HOUR:_____

Appendix B

Data Collection Tool

Appendix B
Data Collection Tool

Granisetron Effectiveness on Postoperative Nausea and Vomiting and the Need for Rescue Antiemetics Data Collection Tool

Study number_____

Age_____

Height_____ft._____in.

Weight_____kg.

Sex____(1)Female____(0)Male

Operative Time_____min.

Recovery Room Time_____min.

ASA Class___I___II___III___IV

Surgical Procedure ICD.9:
_____51.22(Chole)_____68.4(Hys)

History of PONV:
_____(1)Yes_____(0)No

Anesthesia Type:
___(1)Gen___(2)Spinal___(3)Epi

Morphine for Pain Control:
_____(1)Yes_____(0)No

Intraoperative Antiemetics:
___(1)Granisetron
___(2)Dexamethasone
___(3)Promethazine
___(4)Prochlorperazine
___(5)Ondansetron
___(6)Droperidol
___(7)Metoclopramide

PACU Antiemetics:
___(1)Granisetron
___(2)Dexamethasone
___(3)Promethazine
___(4)Prochlorperazine
___(5)Ondansetron
___(6)Droperidol
___(7)Metoclopramide

Nrsg Floor Antiemetics
___(1)Granisetron
___(2)Dexamethasone
___(3)Promethazine
___(4)Prochlorperazine
___(5)Ondansetron
___(6)Droperidol
___(7)Metoclopramide

Home Medications for heartburn/GERD:
___(1)Tums/Rolaids
___(2)Prevacid
___(3)Protonix
___(4)Nexium
___(5)Pepcid
___(6)Other