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Post-Operatives Nausea and Vomiting Treatment in the Adult Surgical Patient

Christine M. Nelson

POSTOPERATIVE NAUSEA AND VOMITING TREATMENT IN THE ADULT SURGICAL PATIENT

By

Christine M. Nelson
Bachelor of Science in Nursing, Minot State University, 2006

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ABSTRACT

The problem of postoperative nausea and vomiting (PONV) in the adult surgical patient continues to be a major source of frustration for both clinicians and surgical patients despite multiple treatment modalities available to allay this problem. PONV can cause patient anxiety in the preoperative period and discomfort in the postoperative period. Multiple pharmacological treatments have been investigated in regard to their efficacy. These treatments have been examined as both single agents and multiple agents in terms of their effectiveness in the adult surgical patient. It is desirable to establish which treatment, whether it is single agent pharmacological treatment or multiple agent pharmacological treatment, is the most effective in preventing PONV. The purpose of this independent project is to consider the efficacy of single pharmaceutical treatment modalities compared to multiple pharmaceutical treatments in preventing and treating PONV in the adult surgical patient. A review and critique of recent literature has been conducted in order to determine the best treatment for PONV. A thorough review of current literature will provide information on single pharmaceutical modalities and combination pharmaceutical modalities that contribute to lowering the risk of PONV. No one pharmacological treatment, whether it is single agent or multiple agents, has been shown to completely prevent PONV.

CHAPTER I

INTRODUCTION

Introduction

For many surgical patients, the preoperative period can be filled with apprehension and anxiety. Fear of the unknown, both during the procedure and after, can fill the surgical patient with unfathomable concern. Of the common complications associated with surgical procedures, postoperative and postdischarge nausea and vomiting is one of the most dreaded. It is reported that this common complication causes more trepidation than postoperative pain (Wender, 2009).

The problem of postoperative nausea and vomiting (PONV) and postdischarge nausea and vomiting (PDNV) affects approximately 25 million people worldwide. The cost implication of this is several million dollars annually (Wender, 2009). In order to better care for surgical patients in the postoperative time period, it is necessary to review treatment modalities for PONV. Although a number of randomized control trials have examined the efficacy of assorted pharmaceutical interventions, and guidelines have been established by both the American Society of Anesthesiologists (ASA) and the American Society of Perianesthesia Nurses (ASPAN), division remains in naming the most effective pharmaceutical treatment.

Purpose of the Project

The purpose of this independent project is to examine the efficacy of single pharmaceutical treatment modalities compared to multiple pharmaceutical treatments in preventing and treating PONV in the adult surgical patient. Many patients are receiving either single agent treatment or multiple agent treatment in preventing and treating PONV. Additionally, some patients may not be receiving any treatment at all. To decrease patient anxiety and improve patient outcomes, it is important for clinicians to be aware of the most effective pharmacological treatment for PONV.

Significance of the Clinical Problem

PONV is considered a significant problem in the postoperative period. Overall, the incidence of PONV can range from 20-30% in the adult surgical patient. The incidence can be as high as 80% in the high-risk patient (Murphy, 2006). Costs incurred in the healthcare system are estimated in the several millions of dollars (Wender, 2009). In a study by van den Bosch et al. (2006), it was determined that patients are willing to put a price tag on preventing PONV.

As a responsible member of the health care team, it is the certified registered nurse anesthetist's (CRNA) goal to manage the surgical patient's care and keep the patient comfortable in the perioperative period. Consequently, during the operative and the postoperative period, it is important for the CRNA to anticipate the patient's need for preventative antiemetic treatment. This preventative treatment may be in the form of adequate fluid volume, preoperative fasting, supplemental oxygen or pharmaceutical agents. There are also a

number of complementary approaches such as aromatherapy, acupressure, guided imagery and music therapy. For the purpose of this review, only preventative pharmacological approaches will be compared. The preventative treatment of PONV may be attempted with single or multiple pharmaceutical agents. It is the intention of this independent project to identify the most efficacious pharmacological treatment whether it is single or multiple agent use.

Assumptions/Limitations

This independent project has assumptions and limitations. It is assumed the CRNA will provide the most comfortable surgical experience possible for the patient. This includes the avoidance of PONV. It is also assumed that certain patients will be at increased risk for PONV, and some patients may not experience this malaise altogether. Patients will prefer to avoid PONV, and the avoidance of such will improve patient satisfaction and promote faster recovery times. If the patient can be given reassurance that every intervention will be attempted to avoid PONV, anxiety will be reduced in regards to PONV.

The unique response of the individual patient to pharmacological treatment can be considered a limitation. Not every patient will respond to treatment as expected, and it is possible that a patient will show no benefit at all to treatment.

Conceptual/Theoretical Framework

The theoretical framework that guided this independent project is Florence Nightingale's environmental adaptation model. Nightingale's model of nursing theory focused on the environment of the patient, which ultimately leads to

patient comfort. Patient comfort, in turn, contributes to healing.

In Nightingale's *Notes on Nursing: What it is and What it is Not* (1912), she used empirical evidence to develop patient care guidelines. These guidelines were researched extensively and developed by Nightingale during her time spent in Turkey during the Crimean War. Nightingale developed her theory long before the establishment of nursing's metaparadigm concepts. According to McEwen and Wills (2006), the metaparadigm concept of nursing includes human, environment, nursing and health. Nightingale specifically addressed cleanliness, fresh air, sanitation, comfort and socialization in *Notes on Nursing*. Of the many notions of nursing she addressed, patient comfort was a key factor.

Nightingale defined the concepts of her philosophy through examples rooted in observation. Although she had used statistical information and kept extensive records, mathematical data did not reach her *Notes on Nursing* (1912). Nightingale focused her writing on empirical evidence. She addressed and defended each concept of her philosophy through example: (a) fresh air prevents stagnation; (b) cleanliness and sanitation promote good health; (c) comfort aids in recovery; (d) socialization may or may not be conducive to therapy. Nightingale addressed these concepts, identifying what worked and what failed to facilitate healing (Nightingale, 1912).

For the surgical patient, comfort can take many forms. Comfort can be found in knowing the patient's health will be either improved or approaching improved, after the surgical procedure is performed. A patient may also take comfort in knowing that the perioperative period will be free of complications such

as anxiety, pain, dry mouth, nausea or vomiting. Avoiding nausea and vomiting in the postoperative period improves the patient's comfort level. This, in turn, hastens the patient's recovery time and promotes healing. If the surgical patient can be assured that the clinician is using the best possible pharmacologic interventions to prevent PONV, anxiety in the preoperative period can be lessened. Less patient anxiety leads to improved patient comfort. Identifying a specific pharmaceutical agent or combination of agents that will keep the surgical patient free of nausea and vomiting will decrease recovery times and improve patient comfort in the postoperative period.

Key Definitions Related to the Clinical Problem

For the purpose of this study, the following definitions are provided.

Antiemetic. A pharmacological agent that reduces or eliminates the sensation of nausea or prevents the act of vomiting.

Nausea. The unpleasant sensation of feeling sick, usually felt prior to vomiting.

Vomiting. The physical act of retching or expelling contents of the stomach.

Postoperative Nausea and Vomiting. Nausea or vomiting that occurs within the first 24 hours following a surgical procedure.

Chapter Summary

The treatment of PONV is a frustrating topic for clinicians. Avoiding additional healthcare costs and improving patient comfort are both reasons for exploring PONV treatment options. Using Nightingale's environmental adaptation model, it the purpose of this independent project to determine the efficacy of single pharmaceutical treatment modalities compared to multiple

pharmaceutical treatments in preventing and treating PONV in the adult surgical patient. While focusing on patient comfort, it should be the goal of the clinician to prevent PONV. Preventing and treating PONV in the perioperative period can improve patient comfort and patient outcomes.

CHAPTER II

REVIEW OF LITERATURE

Introduction

The following is a review and critique of studies related to the topic of postoperative nausea and vomiting (PONV). Risk factors for PONV differ slightly from source to source and will be examined. A number of randomized control studies have been conducted comparing differing pharmacological treatment modalities. The most recent of these will be compared and contrasted. An integrated review from the Cochrane Database of Systematic Reviews was also reviewed. This review looked at eight different antiemetics and compared randomized control trials in which the same antiemetics were observed for their effectiveness in the treatment of PONV.

Search Strategy

In order to conduct a thorough review of the current literature, The Cochrane Library, PubMed (1948 to February 2009) and CINAHL (1982 to February 2009) were searched. The terms used included: "postoperative nausea and vomiting", "nausea and vomiting" and "treatment of nausea and vomiting". The Medical Subject Headings (MeSH) terms that were used include, "postoperative nausea and vomiting", "nausea and vomiting, postoperative", and "agents, antiemetics". The subheadings used were "analysis", "drug therapy", and "prevention and control". The search was limited to journal articles released

within the past ten years, written in English and pertaining to the adult surgical patient. Articles concerning nausea and vomiting in the pediatric surgical patient, the pregnant patient and the oncology patient were not considered for review.

Review and Critique of Related Studies

Postoperative nausea and vomiting may occur for a number of reasons. Drugs and toxins may contribute to development of nausea and vomiting in the surgical patient. The pathophysiology of nausea and vomiting can be traced to the vomiting center of the brain; an anatomical area located in the lateral reticular formation of the medulla. Three nuclei comprise this area, the nucleus tractus solitarius, the dorsal motor nucleus of the vagus, and the nucleus ambiguus. The nucleus tractus solitarius receives sensory information from five primary afferent pathways. Both the dorsal motor nucleus and the nucleus ambiguus coordinate the motor activity for the act of vomiting (Couture, Maye, O'Brien, & Smith, 2006).

The five primary afferent pathways that stimulate the vomiting center vary in their mechanisms. The first pathway, the chemoreceptor-triggering zone (CTZ), is located in the area postrema. This area is found in the lateral walls of the fourth ventricle. Dopamine and serotonin ($5\text{-}HT_3$) in blood and cerebral spinal fluid, opioids and some anesthetic agents stimulate this area. Serotonin can be released from the gastrointestinal tract. The second pathway, the vagal afferent pathway, senses ischemia in the intestine and volume in the stomach. Small changes in the stomach or intestine may set off the vomiting center. Thirdly, the vestibular system is activated through sudden movements of the

head. The reflex afferent pathway activates the vomiting center due to stimulation from anxiety and pain. It also activates the center through visual, sensory and cognitive overload. Finally, the midbrain afferent pathway stimulates the vomiting center through changes in intracranial pressure (Couture et al., 2006). Depending on the type of surgery, or medications used during that surgery, one or more of these afferent pathways can lead to PONV.

Postoperative nausea and vomiting can contribute to a number of objectionable patient outcomes. Patient discomfort, suture dehiscence, aspiration, esophageal rupture, subcutaneous emphysema and prolonged post anesthesia care unit stays are among the complications of this unpleasant event. When a patient must be treated for PONV, the patient's cost of care can increase due to increased amounts of medication required, increased need for nursing care, and a same-day procedure may turn into an overnight admission. The estimated annual cost of PONV in the United States is several hundred million dollars (Kapoor, Hola, Adamson, & Mathis, 2008).

Prophylactic treatment of PONV has been shown to improve patient satisfaction. It may also speed recovery. Prophylactic treatment refers to pharmacological treatment, which is given prior to the postoperative period when symptoms manifest themselves. Treatment can be administered during the operative period at the beginning and end of the case. This may be especially useful in patients who are observed to be at increased risk for PONV (White, Sacan, Nuangchamnong, Sun, & Eng, 2008).

A number of risk factors have been identified the contribute to the

development of PONV. These risk factors can be used to determine which patients are at increased risk for nausea and vomiting. These risk factors can be clustered as patient-specific, anesthetic-related, and surgery-related. Patient-specific risk factors include female gender, nonsmoking, history of PONV, and history of motion sickness (Murphy, Hooper, Sullivan, Clifford, & Apfel, 2006; Kapoor et al., 2008). Anesthetic-related factors include use of volatile anesthetics, use of nitrous oxide, the postoperative use of opioids, and the duration of anesthesia. Surgery-related factors are duration of surgery and type of surgery (Murphy et al., 2006). Specific types of surgery, which lead to increased incidence of PONV, are strabismus surgery, ear surgery, laparoscopy, orchiopexy (surgical movement of an undescended testicle into the scrotum), ovum retrieval, and tonsillectomy (Morgan, Mikhail, & Murray, 2006).

Apfel, Laara, Koivuranta, Greim, and Roewer (1999) developed a simplified risk score that could be used to predict a patient's postoperative risk of PONV. The risk factors specifically focused on were nonsmoking status, female gender, history of PONV or motion sickness, and use of opioid analgesics postoperatively. Each factor associated with the patient in question is given a score of one. A score of 0-4 can be assigned to the individual patient. The assigned risk of PONV is 10%, 21%, 39%, 61% and 79% for a score of 0, 1, 2, 3, and 4, respectively. The average incidence of PONV in surgical patients is 20-30% (Murphy et al., 2006). This risk score has been used in a number of studies to associate risk with efficacy of prophylactic antiemetic treatment. This method of gauging a patient's risk is known as the Apfel score.

White et al. (2008) conducted a study in which risk factors were used to evaluate a patient's risk for developing nausea or vomiting in the first 24 hours of the postoperative period. The Apfel scoring method was used on 130 patients undergoing plastic or laparoscopic surgery. Ninety percent (n=55) of the patients who scored a three in the Apfel scoring method received prophylactic antiemetic treatment. Fifty-six percent of these patients received two or more antiemetics. Ninety-five percent (n=35) of the patients who scored an Apfel four, received antiemetics. Seventy-five percent of these patients received two or more antiemetics. Eleven percent (n=7) of the patients scoring a three suffered from vomiting in the first 6 hours postoperatively. Twenty-two percent (n=8) of the patients scoring a four suffered from vomiting in the first 6 hours postoperatively. Of the patients who scored a two in the Apfel scoring method, 87% (n=28) received antiemetics. Only 6% of the total number of patients scoring a two, suffered from vomiting in the first 6 hours postoperatively. The results of this study conclude that despite multiple antiemetic treatments in those patients with higher Apfel risk scores, the patients were still at increased risk for vomiting.

The American Society of Perianesthesia Nurses (ASPAN) (2006) has developed a guideline for anesthesia care team members that employs the Apfel scoring method. The authors use another tool that considers the length of surgery. With this new tool, an additional one point would be assigned to patients who would be undergoing a procedure that would last more than 60 minutes. The scoring rubric would include

- patients with a score of zero to one would be at a 10-20% risk of experiencing PONV (low risk);
- a score of two would indicate a risk of 40% (moderate risk);
- a score of three would correlate with a 60% chance of PONV (severe risk);
- a score of four to five would indicate a greater than 80% chance of PONV (very severe risk).

The ASPAN guideline indicates (a) patients with low risk should receive no prophylactic antiemetic interventions; (b) patients with moderate risk should receive one intervention; (c) those with severe risk should receive two interventions; (d) those with very severe risk should receive three or more interventions.

The ASPAN guideline describes interventions as pharmacologic considerations, anesthesia considerations and other considerations. Pharmacologic considerations include dexamethasone, serotonin receptor antagonists, histamine receptor blockers, a scopolamine patch or droperidol (see Table 1).

Dexamethasone is a corticosteroid that works as an antiemetic, although its precise mechanism of action is unknown. It is postulated that it enhances the action of 5-HT_3 receptor antagonists. Serotonin receptor antagonists include ondansetron, granisetron, dolasetron, tropisetron, and palonsetron. The 5-HT_3 receptor antagonists work by blocking 5-HT_3 receptors in the gastrointestinal (GI) tract, CTZ and the nucleus tractus solitarius. Promethazine, prochlorperazine, and cyclizine are histamine receptor blockers. These agents block acetylcholine

receptors in the vestibular apparatus of the nucleus tractus solitarius. In addition, promethazine inhibits dopamine and muscarinic receptors. Dopamine is responsible for stimulating the CTZ and the area postrema. Muscarinic receptors are located in the cerebral cortex and pons. Droperidol also blocks dopamine receptors. A scopolamine patch is similar to promethazine in its action by antagonizing muscarinic, cholinergic receptors (Kloth, 2009).

Anesthesia considerations include using total intravenous anesthesia (TIVA), regional blocks or non-steroidal anti-inflammatory drugs. Miller et al. (2005) explains TIVA as the use of propofol (an alkylphenol compound) in conjunction with analgesic agents to achieve general anesthesia. Propofol's pharmacology is attributed to its affect on γ-aminobutyric acid (GABA). GABA has powerful inhibitory affects on the central nervous system. Propofol potentiates the effects of GABA and leads to a hypnotic state (Miller et al., 2005). Other considerations include improving a patient's hydration status (intravenous fluid administration), multi-modal pain management and the stimulation of the P6 acupressure point (ASPAN, 2006). The guideline recognizes there is a need for additional research as to the effectiveness in controlling PONV.

Pharmacologic recommendations similar to the ASPAN algorithm are presented in a literature review by Golembiewski and Tokumaru (2006). However, Golembiewski and Tokumaru go further to describe combinations of antiemetics that should be administered to high-risk patients. Their recommendations also use the Apfel risk score and define severe risk and very severe risk as those patients who score a three and four, respectively. They

define these two risk groups combined as high-risk. If the high-risk group was to undergo surgery using propofol and avoid nitrous oxide (a volatile, inhaled anesthetic gas) and they were given one, two or three antiemetics, the risk would be reduced from 52% to 37%, 28% and 22%, respectively. They assert that the number of prophylactic antiemetics given should increase with the patient's increased risk.

Antiemetics are not free of side effects. One may gain favor over another in the clinician's eyes due to its individual side effect profile. The dopamine receptor blockers (droperidol and metoclopromide) may cause sedation, restlessness and extrapyramidal reactions. In addition, droperidol can cause hypotension, tachycardia, dystonic reactions, anxiety, urinary retention, and prolongation of the QT interval on electrocardiogram. Antihistamines (cyclizine, prochlorperazine and promethazine) can lead to marked sedation, urinary retention and dry mouth. Hypotension, extrapyramidal reactions, tachycardia and restlessness are also possible with prochlorperazine and promethazine. Anticholinergics such as the scopolamine patch may produce hallucinations, urinary retention, restlessness, sedation, dry mouth, visual disturbances, memory loss, and confusion. The 5-HT_3 antagonists (ondansetron, granisetron, dolasetron, tropisetron and palonsetron) have less sedative properties than other agents (Rodriguez & Candiotti, 2009). Slowing of the cytochrome P450 system, which is responsible for the metabolism of other medications such as coumadin and oral contraceptives, is a consequence of using aprepitant, a neurokinin –1 antagonist (Apfel et al., 2008).

The choice of prophylactic antiemetics and in what combination is examined by several studies. The American Society of Anesthesiologists (ASA) (2002) released a guideline outlining the specific antiemetic that a patient should receive as monotherapy and as combination therapy. There are a number of types of antiemetics (see Table 1). According to the ASA, for monotherapy, a 5-HT_3 antagonist, droperidol, dexamethasone or metclopromide should be given. For combination therapy, a 5-HT_3 antagonist with dexamethasone has been found to be the most effective. If a patient has received an antiemetic and requires a rescue antiemetic later in the postoperative period, the ASA (2002) recommends a 5-HT_3 antagonist as the first line agent, regardless if the patient received a 5-HT_3 antagonist initially. However, Ignoffo (2009) reported that the efficacy of this treatment is questionable. Ignoffo's 2009 study suggests that repeat dosing does not have an additional antiemetic effect.

Kloth (2009) agreed that administering multiple agents from the same drug class does not benefit the patient in preventing PONV. This conclusion was from a literature review of new pharmacologic findings in reference to PONV. Depending on the class of antiemetic, if an agent has been given appropriately, that receptor site will be blocked in the body and the administration of a medication from the same class will not improve efficacy. Kloth (2009) does note, however, that there is new data on a 5-HT_3 antagonist called palonsetron. Palonsetron is a second-generation 5-HT_3 antagonist that has improved efficacy when compared to ondansetron in randomized control trials.

Other studies have been conducted on added prophylaxis. Dexamethasone has been shown to decrease the incidence of PONV in the laparoscopic cholecystectomy patient. In a meta-analysis of 17 randomized control trials; the results are the same when dexamethasone is administered along with other antiemetics. However, this meta-analysis found that higher doses (8-16 mg) are associated with less PONV when compared to lower doses (2-5 mg). These findings may especially useful to the high-risk patient (Karanicolas, Smith, Kanbur, Davies & Guyatt, 2008).

A scopolamine patch is another pharmacologic intervention that has been studied when added to ondansetron. According to Jones et al. (2006), in a double blind, randomized, placebo-controlled study, the addition of a scopolamine patch to patients already receiving ondansetron reduced the incidence of PONV. Twenty-five percent (n=7) of patients who received ondansetron and a placebo (n=28) reported "no nausea". Whereas, 61% (n=17) of patients who received ondansetron and a scopolamine patch (n=28) reported "no nausea". The *p* value for this comparison is 0.007. All 56 patients who participated in this study were classified as high-risk. This study did not control for surgical procedure or gender and had a small sample size.

Neurokinin-1 receptor antagonists have recently been found to be effective in combating PONV. According to Apfel, Malhotra and Leslie (2008), neurokinin-1 receptor antagonists prevent the binding of Substance P to neurokinin receptors. Substance P is responsible for stimulating the vomiting center through its binding to cells in the gastrointestinal tract. Treatment with a

neurokinin-1 receptor antagonist showed to reduce the incidence of vomiting by 72% when compared to a placebo (22%). Aprepitant is the first FDA approved neurokinin-1 receptor antagonist. In a three-arm North American multicenter study of ondansetron (4 mg, intravenously), aprepitant (40 mg, oral) and aprepitant (125 mg, oral), the incidence of vomiting was 26, 10 and 5% respectively. This would make aprepitant much more effective than ondansetron (Apfel et al., 2008).

This randomized, double blind comparison (n=766) reveals aprepitant is more effective in the first 48hours postoperatively. However, in the first 24 hours following surgery, no difference is seen in the effects of ondansetron (4 mg, intravenously), aprepitant (40 mg, oral) and aprepitant (125 mg, oral). In the first 24 hours, 42% (n=253) of the patients receiving ondansetron did not require rescue antiemetics or have vomiting. Forty-five percent (n=261) of the patients receiving 40 mg of aprepitant orally did not require rescue antiemetics or have vomiting. Similarly, 43% (n=252) of the patients receiving 125 mg of aprepitant did not require rescue antiemetics or have vomiting ($P>0.5$ for both odds ratios). This positive result in the later postoperative period may be explained by the difference in half-life. The half-life of ondansetron is 4-9 hours and 9-12 hours for aprepitant (Gan et al., 2007). The effect of aprepitant when combined with other antiemetics was not investigated. This information would be valuable in the treatment of PONV with multiple agents.

Table 1

Classification of Antiemetics and Drug Names

Class of Antiemetic	Drug	
	Generic	Trade Name
Serotonin receptor 3 (5-HT_3) antagonists	ondansetron	Zofran®
	granisetron	Kytril®
	dolasetron	Anzemet®
	tropisetron	Navoban®
	palonsetron	Aloxi®
Dopamine receptor blockers	droperidol	Inapsine®
	metoclopromide	Reglan®
Antihistamines	cyclizine	Antivert®
	prochlorperazine	Compazine®
	promethazine	Phenergan®
Glucocorticoid	dexamethasone	Decadron®
Anticholinergics	scopolamine patch	Transderm Scop®
Neurokinin –1 receptor antagonists	aprepitant	Emend®

In a prospective, randomized, double-blind study by Jellish, Owen, Fluder, Sawicki, and Sinacore (2009), patients undergoing abdominal surgery and having patient controlled analgesia (PCA) following surgery, were given ondansetron, a combination of ondansetron and prochlorperazine or no antiemetic. The antiemetics were administered through the PCA, intravenously. The patients who received no antiemetic had a 49% incidence of PONV. The patients, who received ondansetron alone, had an incidence of PONV of 38%. The patients, who received ondansetron and prochlorperazine together, had an incidence of PONV of 29%. This study could be further extrapolated to research the addition of other combinations of antiemetics to patients' PCAs.

In 2004, a large, randomized, controlled trial of factorial design conducted by Apfel et al., compared ondansetron, dexamethasone, and droperidol side by side. In addition, the researchers compared six prophylactic interventions (a) 4 mg of ondansetron or no ondansetron; (b) 4 mg of dexamethasone or no dexamethasone; (c) 1.25 mg of droperidol or no droperidol; (d) propofol or a volatile anesthetic; (e) nitrogen or nitrous oxide; (f) remifentanil or fentanyl. A total of 5199 patients were involved in the study, of which, 4123 were randomly assigned to receive 1 of 64 possible combinations of prophylaxis. The remaining patients were randomly assigned combinations of the first four interventions. All patients who were involved in the trial were considered to have a PONV risk of at least 40%. The trial showed ondansetron lowered the risk of PONV by 26% ($P<0.001$); dexamethasone lowered the risk by 26.4% ($P<0.001$); and droperidol lowered the risk by 24.5% ($P<0.001$). When antiemetics are given together, their

effects are additive. The most effective treatment would be to give all three medications. There was a 26% risk reduction for the addition of each antiemetic. However, a significant difference could not be seen among any pair of antiemetics (P=0.81).

A large systematic review was conducted by Carlisle and Stevenson (2004) for the Cochrane Database of Systematic Reviews. This review compared 737 studies, and identified eight drugs that, when compared to placebos, were efficacious in preventing PONV. These drugs were droperidol, metclopromide, ondansetron, tropisetron, dolasetron, dexamethasone, cyclizine, and granisetron. The efficacies of the drugs varied and it is reported that publication bias makes it difficult to reliably disseminate which drug is more effective than another. This bias stems from numerous inconsistencies in the 737 studies included. Two hundred seventy-six studies included sample size, 461 did not. In 550 studies, the authors do not reveal how the sample groups were allocated. Anesthesiologists administering pharmacological interventions were not blinded in 447 studies. Finally, 231 studies did not follow up with patients.

Carlisle and Stevenson reported that either nausea or vomiting affects 80% of surgical patients. If every surgical patient were given an antiemetic, only 28% would show a benefit to treatment. According to this review, there was convincing evidence that when droperidol is administered it is more effective when more of the drug is given. Similar efficacy results were found for dexamethasone and ondansetron only with limited evidence. The review does

not specify what doses are appropriate. The review does list further implications for research. It does not list combination treatment as a future research area. This review questions the side effect profile of antiemetics versus their efficacy.

Summary of the Review of Literature

In reviewing the literature regarding PONV, it is evident there is further need for the study of antiemetic treatment either in combination or as monotherapy. Although a number of treatments, both pharmacological and other may be employed, and guidelines have been developed, there is not a truly effective treatment for PONV. There are a number of pharmacological agents available, each effective to some extent, proving to be more effective in combination. Following the guidelines developed by the ASPAN and the ASA may guide the most effective treatment due to their focus on multiple modalities.

Chapter Summary

Although a specific single agent or multiple agent pharmacological intervention has not been identified to completely prevent or treat PONV, a number of treatments have been recognized for their effectiveness compared to other treatments. A large number of studies have been conducted to compare pharmacological agents to one another and compare different doses in the same drug for their efficacy. Although efforts to identify the optimal treatment based on a patients risk stratification have been attempted, it is evident there cannot be a specific treatment that is successful in completely eliminating PONV.

CHAPTER III

METHODS

Introduction

The problem of postoperative nausea and vomiting (PONV) is well established. It is in the best interest of the clinician to avoid PONV to improve patient satisfaction and curtail costs incurred to the healthcare system. In addition to non-pharmacological interventions, the clinician should be informed on recent research on the effectiveness of pharmacological interventions. In order to address this problem, it is necessary to educate providers, specifically, Certified Registered Nurse Anesthetists and Student Registered Nurse Anesthetists.

Target Audience

The target audience for this independent project was Student Registered Nurse Anesthetists (SRNA), Certified Registered Nurse Anesthetists (CRNA), and CRNA faculty. This independent project was presented in the format of PowerPoint™ presentation (Appendix A). It was presented to first-year, second-semester anesthesia students at the University of North Dakota in the fall of 2009. It was also presented to CRNAs and SRNAs attending the North Dakota Association of Nurse Anesthetists Spring Assembly in Fargo, North Dakota. An evaluation tool was used to determine the presentation's effectiveness when presented to SRNAs (Appendix B).

Procedures

To provide a complete synopsis of the review of literature conducted on the topic of PONV in the adult surgical patient, a PowerPoint™ presentation was developed. This presentation included an overview of the physiology of nausea and vomiting. It also included information on each antiemetic including its mechanism of action, side effect profile and efficacy in comparison to other antiemetics. A review of current literature was also included.

The program director of the University of North Dakota Nurse Anesthesia Specialization was contacted in regard to presenting the PowerPoint™ presentation as an in-service to first year students. The project was presented on December 2, 2009. Questions, comments, and candid discussion concerning presentation content and personal clinical experiences were encouraged.

Evaluation

The presentation of this independent project was assessed using a guest speaker evaluation form (Appendix B). A Likert scale was employed to evaluate the effectiveness of the proposed presentation. A score of five indicated the audience member strongly agreed with the statement. Six statements were used to evaluate the presentation. Comments were encouraged regarding speaker and program strengths, suggestions for improvement, and additional comments through open-ended items on the evaluation form.

Chapter Summary

Presenting current information on PONV to SRNAs and CRNAs will increase the appropriate use of risk assessment tools and pharmacologic antiemetic agents in practice. When clinicians are up to date on current practices and recommendations, patient satisfaction will be improved. A PowerPoint™ presentation serves as an efficient means of presenting information in an organized format. The use of an evaluation tool aids in determining the effectiveness of the presentation.

CHAPTER IV

RESULTS AND IMPLICATIONS

Introduction

In order to evaluate the effectiveness of the PowerPoint™ presentation, the results from the guest speaker evaluation form were assessed. The evaluation form was provided to all twelve of the SRNAs of whom the information was presented. Twelve forms were completed and collected following the presentation. A value of five, or strongly agree was given by all twelve students in the areas of "The program length was appropriate for the subject matter.", and "I would recommend this presentation to other students.". A five was also given by eleven students on the remaining four statements, with one student assigning a four to each of those statements. In the area for suggestions for improvement, it was mentioned the font on the slides was too small and the cost of antiemetics could be explored. Additionally, only positive comments were received in the area for speaker strengths and additional comments. Comments included mention of the usefulness of this topic in practice, the ease and comfort of the speaker and that the topic was considered interesting. Students were encouraged to share their thoughts and clinical experiences following the presentation and many participated.

The presentation was well received by the students. As evidenced by the speaker evaluation results, the students will use this information in their practice

and they benefited from the information. They were receptive and attentive during the presentation and participatory in the open discussion that followed. They were also appreciative of the information provided.

Information regarding the avoidance of PONV in the adult surgical patient has many implications. Reviewing current information can influence the areas of nursing practice, education, research, and policy.

Nursing Practice

Providing comfort in the perioperative period can be an overwhelming task for healthcare providers. Patients can be especially concerned with the postoperative period. These concerns are not unfounded as PONV is a threat to patient comfort. While PONV may not be completely avoidable in all patients, there is adequate evidence to guide the practitioner's choice of interventions, and stratify a patient's risk. With the adoption of the ASPAN's guideline, many surgical facilities could implement a strategy usable by all practitioners to guide patient treatment of PONV. Those patients with the highest risk are identified early, and interventions can be initiated prior to an emetic event. Ultimately, successful treatment will lead to improved patient satisfaction and shortened hospital stays.

Nursing Education

Education in regards to pharmacological interventions for the prevention of PONV should be presented early and often in the didactic path of the practitioner. In order to provide the best care possible and improve patient satisfaction, the practitioner should strive to stay informed of current treatments and

recommendations regarding this topic. This can be accomplished through early introduction of the pathophysiology behind the emetic response, and the pharmacological interventions proven to prevent this malaise. Continuing education is also an important part of the competent practitioner's responsibility. The patient only stands to benefit when evidence-based practice is employed.

Nursing Research

While much research has focused on the efficacy of various antiemetic treatments, both alone and in combination, a clear, effective pharmacological intervention remains to be identified. Clinicians must use evidenced-based practice to guide their decisions regarding selection of one or more antiemetics, and in stratifying the patient's risk for PONV. A responsible clinician must also seek out new research involving the effectiveness of pharmacologic agents. There are opportunities for continued research of pharmacologic agents used for treatment of PONV. These areas of opportunity include investigating the use of different drug combinations, side-by-side comparison of one agent versus another and the effectiveness of risk assessments.

Nursing Policy

Effective nursing policy insures the delivery of quality patient care. Guidelines have been established by the ASPAN. By using these guidelines, it may be possible for practitioners to identify which patients have a higher risk of PONV than others. Interventions can then be considered and incorporated into the patient's plan of care. While individual clinicians may make decisions based on their personal experience, it would be beneficial for healthcare institutions to

have a standard policy and procedure for the treatment of PONV in the adult surgical patient. The ASA has developed guidelines for the selection of pharmacologic agents. These guidelines may ensure continuity of care from patient to patient.

Chapter Summary

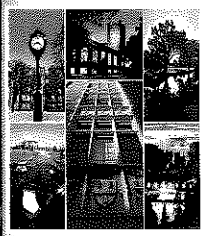
The avoidance of PONV in the adult surgical patient has the potential to improve patient satisfaction and lower healthcare costs. While there are areas of research that may need further investigation, there are pharmacologic agents that have been identified as being effective. The use of evidence-based practice improves the quality and continuity of patient care. It is imperative that clinicians and students stay abreast of current antiemetic treatments and their level of effectiveness. Policy implementation will also lead to improved patient satisfaction when those policies are used effectively. These tasks can be achieved by considering the risk assessment tools available, such as the Apfel score. In addition, recommendations made by the American Society of Perianesthesia Nurses and the American Society of Anesthesiologists can be followed in anticipation of avoiding or decreasing the risk of PONV in at-risk patients. Randomized controlled trials have also provided guidance on antiemetic treatments. While no one treatment or combination of treatments has been recognized as being thoroughly effective, suggestions offered by these entities can be used in clinical practice to guide quality patient care.

APPENDICES

Appendix A

PowerPoint™ Presentation

Postoperative Nausea and Vomiting in the Adult Surgical Patient



Christine Nelson, SRNA
University of North Dakota
December 2, 2009

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Significance

- Overall, the incidence of PONV can range from 20-30% in the adult surgical patient(Murphy, 2006).
- The incidence can be as high as 80% in the high-risk patient (Murphy, 2006).
- Costs incurred in the healthcare system are estimated in the several millions of dollars (Wender, 2009)
- In a study by van den Bosch, et al (2006), it was determined that patients are willing to put a price tag on preventing PONV .

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Purpose

- The purpose of this independent project is to examine the efficacy of single pharmaceutical treatment modalities compared to multiple pharmaceutical treatments in preventing and treating PONV in the adult surgical patient.

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Problem

- Patients may be receiving none, one or multiple agents
- To improve patient outcomes and decrease patient anxiety, it is beneficial for clinicians to be aware of current treatment modalities.
- Patient discomfort, suture dehiscence, aspiration, esophageal rupture, subcutaneous emphysema and prolonged post anesthesia care unit stays are among the complications of this unpleasant event.
- When a patient must be treated for PONV, the patient's cost of care can increase due to increased amounts of medication required, increased need for nursing care, and a same-day procedure may turn into an overnight admission.
- The estimated annual cost of PONV in the United States is several hundred million dollars (Kapoor, Hola, Adamson, & Mathis, 2008).

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Objectives

1. Review the pathophysiology of nausea and vomiting.
2. Identify risk factor that contribute to postoperative nausea and vomiting (PONV).
3. Explore scoring methods for PONV.
4. Examine pharmacologic antiemetic treatment's mechanisms of action and side effect profiles.
5. Consider recent research on effective pharmacological treatment of PONV.

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Methods

- A review of literature was performed and data was compiled and compared and contrasted.
- A presentation was prepared for Certified Registered Nurse Anesthetists and Student Registered Nurse Anesthetists.
- Nightingale's environmental adaptation model was used as the theoretical framework to guide this independent project.

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Pathophysiology

- Vomiting center of the brain; an anatomical area located in the lateral reticular formation of the medulla
- Three nuclei: the nucleus tractus solitarius, the dorsal motor nucleus of the vagus, and the nucleus ambiguus
- The nucleus tractus solitarius receives sensory information from five primary afferent pathways. Both the dorsal motor nucleus and the nucleus ambiguus coordinate the motor activity for the act of vomiting (Couture, Maye, O'Brien, & Smith, 2006)

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Related Study

- White et al. (2008) conducted a study in which risk factors were used to evaluate a patient's risk for developing nausea or vomiting in the first 24 hours of the postoperative period.
  - The Apfel scoring method was used, 130 patients undergoing plastic or laparoscopic surgery.
  - 87% (n=28) of the patients who scored a 2 received treatment
    - 6% suffered from vomiting in the first 6 hours
  - 90% (n=55) of the patients who scored a 3 received treatment
    - 56% percent of these patients received two or more antiemetics.
    - 11% (n=7) of the patients scoring a three suffered from vomiting in the first 6 hours postoperatively.
  - 95% (n=35) of the patients who scored a 4 received treatment
    - 75% of these patients received two or more antiemetics
    - 22% (n=8) of the patients scoring a four suffered from vomiting in the first 6 hours postoperatively
  - The results of this study conclude that despite multiple antiemetic treatments in those patients with higher Apfel risk scores, the patients were still at increased risk for vomiting

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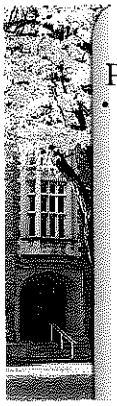

Pathophysiology

- Five Primary afferent pathways:
  - Chemoreceptor-triggering zone (CTZ) - located in the area postrema, found in the lateral walls of the fourth ventricle
    - Dopamine and serotonin ($5\text{-}HT_3$) in blood and cerebral spinal fluid, opioids and some anesthetic agents stimulate this area. Serotonin can be released from the gastrointestinal tract.
  - Vagal afferent pathway - senses ischemia in the intestine and volume in the stomach.
    - Small changes in the stomach or intestine may set off the vomiting center.
  - Vestibular system - activated through sudden movements of the head.
  - Reflex afferent pathway - activates the vomiting center due to stimulation from anxiety and pain
    - It also activates the center through visual, sensory and cognitive overload.
  - Midbrain afferent pathway - stimulates the vomiting center through changes in intracranial pressure (Couture et al., 2006)

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American Society of Perianesthesia Nurses (ASPAN) Scoring (2006)

- Includes an additional point for surgery lasting more than 1 hour
  - 0-1would be at a 10-20% risk of experiencing PONV (**low risk**)
  - 2 would indicate a risk of 40% (**moderate risk**)
  - 3 would correlate with a 60% chance of PONV (**severe risk**)
  - 4-5 would indicate a greater than 80% chance of PONV (**very severe risk**)
- The ASPAN guideline indicates:

a) patients with low risk should receive no prophylactic antiemetic interventions
b) patients with moderate risk should receive one intervention
c) those with severe risk should receive two interventions
d) those with very severe risk should receive three or more interventions.

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Risk Factors

- Patient-specific
  - Female gender, nonsmoking, history of PONV and history of motion sickness
- Anesthesia-related
  - Use of volatile anesthetics, use of nitrous oxide, the postoperative use of opioids and duration of anesthesia
- Surgery-related
  - Strabismus surgery, ear surgery, laparoscopy, orchiopexy, ovum retrieval and tonsillectomy (Morgan, Mikhail, & Murray, 2006)

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ASPAN cont'd

- Pharmocologic considerations
  - dexamethasone, serotonin receptor antagonists, histamine receptor blockers, a scopolamine patch or droperidol
- Anesthesia considerations
  - using total intravenous anesthesia (TIVA), regional blocks or non-steroidal anti-inflammatory drugs
- Other considerations
  - improving a patient's hydration status (intravenous fluid administration), multi-modal pain management and the stimulation of the P6 acupressure point

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Risk Scoring

- Used to predict a patient's postoperative risk of PONV. Known as the Apfel score.
- Focused on specific risk factors of nonsmoking status, female gender, history of PONV or motion sickness and the use of opioid analgesics postoperatively (1 point per factor)
- Score 0-4;0=10%, 1=21%, 2=39%, 3=61% and 4=79% (Apfel et al., 1999)
- The average incidence is 20-30% (Murphy et al., 2006)

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Related Study

- Golembiewski and Tokumaru (2006) define patients scoring a 3 and 4 are defined as high-risk (52% risk of PONV)
- For surgery using propofol (avoiding nitrous oxide), the patients were given
  - 1 antiemetics – risk reduced to 37%
  - 2 antiemetics – risk reduced to 28%
  - 3 antiemetics – risk reduced to 22%
- They assert the number of prophylactic antiemetics given should increase with the patient's increased risk.

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Antiemetics (Pharmocologic agents)

Drug	Class	Mechanism of Action	Side Effects
Dexamethasone	Corticosteroid	Unknown, may enhance the action of 5-HT3 receptor antagonists	very little if one-time dose
Ondansetron, granisetron, dolasetron, tropisetron, palonsetron	Serotonin receptor antagonist	block 5-HT3 receptors in the GI tract, CTZ and the nucleus tract solitarius	less sedative properties than other agents
Promethazine, prochlorperazine, cyclizine	Antihistamine	block acetylcholine receptors in the vestibular apparatus of the nucleus tractus solitarius, promethazine inhibits dopamine and muscarinic receptors	marked sedation, urinary retention and dry mouth; hypotension, extrapyramidal reactions, tachycardia and restlessness are also possible with prochlorperazine and promethazine
Droperidol, metoclopramide	Dopamine receptor blocker	block dopamine receptors	sedation, restlessness and extrapyramidal reactions, droperidol can cause hypotension, tachycardia, dystonic reactions, anxiety, urinary retention and prolongation of the QT interval on electrocardiogram
Scopolamine	Anticholinergic	antagonizes muscarinic, cholinergic receptors	hallucinations, urinary retention, restlessness, sedation, dry mouth, visual disturbances, memory loss, and confusion
Aprepitant	Neurokinin-1 receptor antagonist	neurokinin-1 receptor antagonist	Slowing of the cytochrome P450 system

(Rodriguez & Candiotti, 2009; Apfel et al, 2008; Kloth, 2009)

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However…

- In the first 24 hours, 42% (n=253) of the patients receiving ondansetron did not require rescue antiemetics or have vomiting. Forty-five percent (n=261) of the patients receiving 40 mg of aprepitant orally did not require rescue antiemetics or have vomiting. Similarly, 43% (n=252) of the patients receiving 125 mg of aprepitant did not require rescue antiemetics or have vomiting (P>0.5 for both odds ratios). This positive result in the later postoperative period may be explained by the difference in half-life. The half-life of ondansetron is 4-9 hours and 9-12 hours for aprepitant (Gan et al., 2007).
- The effect of aprepitant when combined with other antiemetic was not investigated. This information would be valuable in the treatment of PONV with multiple agents.

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Other Guidelines

- The American Society of Anesthesiologists (ASA) (2002): for monotherapy, a 5-HT_3 antagonist, droperidol, dexamethasone or metclopromide should be given; for combination therapy, a 5-HT_3 antagonist with dexamethasone has been found to be the most effective; if a patient has received an antiemetic and requires a rescue antiemetic later in the postoperative period, the ASA (2002) recommends a 5-HT_3 antagonist as the first line agent, regardless if the patient received a 5-HT_3 antagonist initially
- Ignoffo (2009) reported that the efficacy of this treatment is questionable.
- Kloth (2009) agreed that administering multiple agents from the same drug class does not benefit the patient in preventing PONV. Depending on the class of antiemetic, if an agent has been given appropriately, that receptor site will be blocked in the body and the administration of a medication from the same class will not improve efficacy.
  - Palonsetron

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Related Studies

- Prospective, randomized, double-blind study by Jellish, Owen, Fluder, Sawicki, and Sinacore (2009), patients undergoing abdominal surgery and having patient controlled analgesia (PCA) following surgery, were given ondansetron, a combination of ondansetron and prochlorperazine or no antiemetic.
- The antiemetics were administered through the PCA, intravenously.
  - No antiemetic: 49% incidence of PONV
  - Ondansetron alone:38% incidence of PONV
  - Ondansetron and prochlorperazine together: 29% incidence of PONV
  - This study could be further extrapolated to research the addition of other combinations of antiemetics to patients' PCAs.

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Related Studies

- Dexamethasone in the laparoscopic cholecystectomy patient: In a meta-analysis of 17 randomized control trials; the results are the same when dexamethasone is administered along with other antiemetics. These findings may especially useful to the high-risk patient (Karanicolas, Smith, Kanbur, Davies and Guyatt, 2008).
- Scopolamine patch with ondansetron: According to Jones et al. (2006), in a double blind, randomized, placebo-controlled study, the addition of a scopolamine patch to patients already receiving ondansetron reduced the incidence of PONV.
  - 25% (n=7) of patients who received ondansetron and a placebo (n=28) reported "no nausea"
  - 61% (n=17) of patients who received ondansetron and a scopolamine patch (n=28) reported "no nausea"
  - P value is 0.007

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Related Studies

- In 2004, a large, randomized, controlled trial of factorial design conducted by Apfel et al., compared ondansetron, dexamethasone, and droperidol side by side. In addition, the researchers compared 6 prophylactic interventions

a) 4 mg of ondansetron or no ondansetron
b) 4 mg of dexamethasone or no dexamethasone
c) 1.25 mg of droperidol or no droperidol
d) propofol or a volatile anesthetic
e) nitrogen or nitrous oxide
f) remifentanil or fentanyl

- A total of 5199 patients were involved in the study, of which 4123 were randomly assigned to receive 1 of 64 possible combinations of prophylaxis. The remaining patients were randomly assigned combinations of the first four interventions.

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Neurokinin-1 Receptor Antagonists

- According to Apfel, Malhotra and Leslie (2008), neurokinin-1 receptor antagonists prevent the binding of Substance P to neurokinin receptors
  - Substance P is responsible for stimulating the vomiting center through its binding to cells in the gastrointestinal tract
- Treatment with a neurokinin-1 receptor antagonist showed to reduce the incidence of vomiting by 72% when compared to a placebo (22%).
- Aprepitant is the first FDA approved neurokinin-1 receptor antagonist.
- In a three-arm North American multicenter study of ondansetron (4 mg, intravenously), aprepitant (40 mg, oral) and aprepitant (125 mg, oral), the incidence of vomiting was 26, 10 and 5% respectively. This would make aprepitant much more effective than ondansetron (Apfel et al., 2008).
- Aprepitant is more effective in the first 48hours postoperatively

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Related Studies

- All patients had a PONV risk of at least 40%.
- The trial showed ondansetron lowered the risk of PONV by 26% (P<0.001); dexamethasone lowered the risk by 26.4% (P<0.001); and droperidol lowered the risk by 24.5% (P<0.001).
- When antiemetics are given together, their effects are additive. The most effective treatment would be to give all three medications. There was a 26% risk reduction for the addition of each antiemetic. However, a significant difference could not be seen among any pair of antiemetics (P=0.81)(Apfel et al., 2004).

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Related Studies

- A large systematic review was conducted by Carlisle and Stevenson (2004) for the Cochrane Database of Systematic Reviews. This review compared 737 studies, and identified eight drugs that, when compared to placebos, were efficacious in preventing PONV.
  - **droperidol, metclopromide, ondansetron, tropisetron, dolasetron, dexamethasone, cyclizine, and granisetron**
  - The efficacies of the drugs varied and it is reported that publication bias makes it difficult to reliably disseminate which drug is more effective than another.
  - This bias stems from numerous inconsistencies in the 737 studies included:
    - 276 studies included sample size, 461 did not
    - 550 studies, the authors do not reveal how the sample groups were allocated
    - Anesthesiologists administering pharmacological interventions were not blinded in 447 studies
    - 231 studies did not follow up with patients.

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Related Studies

- Carlisle and Stevenson reported:
  - either nausea or vomiting affects 80% of surgical patients
  - if every surgical patient were given an antiemetic, only 28% would show a benefit to treatment
  - when droperidol is administered it is more effective when more of the drug is given
  - similar efficacy results were found for dexamethasone and ondansetron only with limited evidence (the review does not specify what doses are appropriate)
- The review does list further implications for research. It does not list combination treatment as a future research area. This review questions the side effect profile of antiemetics versus their efficacy.

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Summary

- In reviewing the literature regarding PONV, it is evident there is further need for the study of antiemetic treatment either in combination or as monotherapy.
- Although a number of treatments, both pharmacological and other may be employed, and guidelines have been developed, there is not a truly effective treatment for PONV.
- There are a number of pharmacological agents available, each effective to some extent, proving to more effective in combination.
- Following the guidelines developed by the ASPAN and the ASA may guide the most effective treatment due to their focus on multiple modalities
- Although a specific single agent or multiple agent pharmacological intervention has not been identified to completely prevent or treat PONV, a number of treatments have been recognized for their effectiveness compared to other treatments.
- A large number of studies have been conducted to compare pharmacological agents to one another and compare different doses in the same drug for their efficacy. Although efforts to identify the optimal treatment based on a patients risk stratification have been attempted, it is evident there cannot be a specific treatment that is successful in completely eliminating PONV.

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Appendix B

Guest Speaker Evaluation Form

University of North Dakota
College of Nursing
Nurse Anesthesia Specialization

GUEST SPEAKER EVALUATION FORM

Name of Guest Speaker **Christine Nelson**

Topic **Postoperative Nausea and Vomiting in the Adult Surgical Patient**

Date of presentation **December 2, 2009**

	Strongly Agree - Disagree				
Please place an X in the appropriate boxes	**5**	**4**	**3**	**2**	**1**
1. The objectives were clearly presented (if applicable)					
2. The content of the speaker's talk met my expectations.					
3. The speaker presented the material in a clear and logical manner.					
4. The program length was appropriate for the subject matter.					
5. I would recommend this presentation to other students.					
6. The material was helpful and will benefit me in my practice.					

Speaker strengths:

Suggestions for improvement:

Additional Comments:

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