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Postoperative Nausea and Vomiting Algorithm Pocket Guide

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POSTOPERATIVE NAUSEA AND VOMITING ALGORITHM POCKET GUIDE

by

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To my loving husband Leon

and beautiful children LaCarra and Lindsey,

without your support and encouragement

this goal would not have been fulfilled

ABSTRACT

Background: Postoperative nausea and vomiting (PONV) remain common complications following surgery and their causes and treatments are complex. Despite much research and advances in treatment, PONV is present as often as 25-30% following all surgical cases. Patients have identified avoidance of nausea and vomiting, avoidance of gagging on endotracheal tube, and control of postoperative pain as their top priorities following surgery. Certain patient characteristics, type of surgery performed, and some anesthetic medications have been implicated in increasing the risk of developing PONV. Patients at high risk for developing PONV are frequently female, have a history of PONV or motion sickness, are nonsmokers, are undergoing laparoscopic procedures, or have received intraoperative and postoperative opiates to control pain. By quickly and effectively identifying patients that are high risk for developing PONV, the CRNA can improve patient satisfaction, minimize postoperative complications and unanticipated hospital admissions, and prioritize therapy in a cost-effective manner. The purpose of this project is to create a pocket guide that can be easily utilized by anesthesia personnel to assess risk for development of PONV and an algorithm that guides decision-making for prophylactic treatment individualized to each patients associated risk.

Methodology: Following an extensive review of the literature, a risk stratification model for PONV was chosen as a screening tool for all patients undergoing surgical procedures. The number and severity of risk factors serves as a guide for the anesthesia

provider in prophylactic therapy decisions for nausea and vomiting. An algorithm based on evidence and consensus, as determined by the literature, was developed. These pocket guides are designed to be used by the novice, advanced beginner, and competent nurse anesthetist.

Conclusions: By having a simple handy guide that can be carried with the anesthesia provider at all times, patients can be quickly and appropriately screened and risk determined. Based upon the level of risk, decisions regarding prophylactic treatment of PONV can be made to meet patients' needs and provide cost effective care.

CHAPTER I

INTRODUCTION

Postoperative nausea and vomiting (PONV), either individually or combined, are common complications following outpatient surgery that have an impact on patients and healthcare institutions. These complications may lead to increased length of stay, overnight admission, and increased costs. Despite many newer medications and increased understanding in the etiology of nausea and vomiting, postoperative nausea and vomiting remains a complex problem in the effective post anesthesia management of patients. PONV is present following 25-30% of all surgical procedures with intractable vomiting occurring in 0.18% of all patients following anesthesia (Kovac, 2000). Following outpatient laparoscopic procedures, 45% of patients were reported to experience ongoing nausea despite prophylactic treatment with Ondansetron, considered the gold standard for PONV prophylaxis (Ahmed, Hobbs, & Curran, 2000).

Factors that effect the incidence of PONV varies depending upon the anesthetic agents, patient characteristics, and types of procedures performed. Women have a three times greater incidence of PONV then men (Sinclair, Chung, & Mezei, 1999). Laparoscopic, abdominal, and gynecological procedures are all associated with an increased incidence of PONV (Kenny, 1994).

Clinical Problem

Postoperative nausea and vomiting is a pervasive problem following general anesthesia and has a complex and multi-factorial etiology. The incidence of PONV is estimated to be as high as 70% following intra-abdominal surgery. Kenny (1994) has described the incidence to be as high as 58% following major gynecological procedures and 40% to 77% following laparoscopic procedures. Kenny (1994) identified factors associated with increased incidence of PONV to include most anesthetic agents and opioids, women and children, patient history of PONV or motion sickness, and patients undergoing abdominal, gynecological, or strabismus surgery.

PONV is frequently so common that it is sometimes considered a consequence of general anesthesia. PONV can have negative effects through decreased patient satisfaction, increased use of medical and nursing time, and increased use of healthcare resources in an attempt to manage it. Patients have strong feelings about PONV and have identified avoiding nausea and vomiting, gagging on the endotracheal tube, and incisional pain control as their top priorities following anesthesia care (Macario, Weinger, Carney, & Kim, 1999).

Certified Registered Nurse Anesthetists (CRNAs) are instrumental in developing and implementing the anesthetic plan for patients undergoing surgical procedures. Anesthetic regimes must safely provide adequate anesthesia, analgesia, and amnesia throughout the entire peri-operative experience. Therefore, the anesthetic plan must include medications to prevent and reduce the incidence of postoperative complications. Since patients at risk for the development of PONV vary depending on patient characteristics, anesthetic factors, and surgical procedures , the CRNA is challenged to find effective and cost efficient ways to manage both postoperative nausea and emesis.

Purpose

The purpose of this project is to develop a pocket style card that can serve as an easy reference for rapid identification, risk stratification, and treatment of patients undergoing anesthesia. Based on determined risk, an algorithm guides the anesthesia provider in choices of antiemetic agents recommended to provide a balanced and cost effective anesthetic regime.

Theoretical Framework

Patricia Benner's *From Novice to Expert: Excellence and Power in Clinical Nursing Practice* provides the theoretical model for which this project is based. Benner formed her theory by studying clinical nursing practice to discover and describe how knowledge in nursing practice is acquired over time and differentiate practical from theoretical knowledge. Benner adapted the Dreyfus Model of Skill Acquisition and Skill Development for application to clinical nursing practice (Benner, 1984). Benner's model describes five levels of skill acquisition and development: (1) novice, (2) advanced beginner, (3) competent, (4) proficient, and (5) expert (Benner, 1984).

A novice is described as a person who has no background experience of the situation in which he/she is participating. Performance is guided by context-free rules and objectives. The novice has difficulty discerning between relevant and irrelevant aspects of a situation. This level of skill acquisition generally applies to students of nursing or an experienced clinician when placed in an unfamiliar situation or environment (Marriner Tomey & Alligood, 2002).

The advanced beginner demonstrates marginally acceptable performance by recognizing the recurring meaningful components of the situation, either by having coped with enough real life situations or having them pointed out by a mentor. Nurses performing in this level are guided by rules, are task oriented, and are challenged to find the larger perspective in the given situation. Clinical situations are viewed from the nurses perspective as a test of there abilities and demands placed upon them, instead of viewing it as patient needs and responses (Benner, Tanner, & Chesla, 1992). Advanced beginners feel managing patient care is their responsibility, but remain dependant upon the assistance of the more experienced nurses. The newly graduated nurse is an example of an advanced beginner (Benner, 1984).

The Dreyfus model has described the competent stage has having increased conscious and purposeful planning that enables one to discern which aspects of current and future situations are important and which can be ignored (Benner, 1984). The nurse progresses to this stage through learning from practice situations and following the actions of others. Benner et al. (1992) identify consistency, predictability, and time management, especially in relation to the nurse's organization versus patient needs, as accomplishments in this stage. Nurses in this stage often demonstrate a hyper-responsibility to the patient and are overly critical of themselves. The competent stage is most important in clinical learning as the nurse begins to prioritize and recognize patterns. The competent nurse begins to develop new ways of doing and rationalize the action while incorporating previous rules based upon the context of the situation (Marriner Tomey & Alligood, 2002).

The proficient stage is considered an extreme transition from competent. The nurse in this stage perceives the situation as a whole versus several smaller aspects that produce a given situation. An intuitive understanding of the situation based upon previous knowledge and experience permits the nurse to recognize the most subtle aspects of a situation. Nurses in this stage have an increased confidence in their knowledge and abilities, and are able to recognize changes in a situation as it evolves. Proficient nurses are able to move beyond how situations affect them and how they effect situations, to have more involvement with the patient and family (Marriner Tomey & Alligood, 2002).

The final stage of the skills acquisition model, expert, occurs when the individual no longer relies on rules, guidelines, or rationales to understand the situation and the appropriate action. It is a way of knowing intuitively what the situation is and what is required without needing to consider alternatives (Marriner Tomey & Alligood, 2002). The expert nurse, drawing upon prior situational learning, identifies the patients needs and concerns as being of utmost concern, recognizes what planning needs to occur, and advocates for the patient (Benner et al., 1992).

Benner further distinguishes advanced beginner and expert by explicating two interrelated aspects of practice. "First, clinicians at different levels of practice function in different clinical worlds, recognized and responding to different situated needs for action" (Marriner Tomey & Alligood, 2002, p.168). Second, clinicians develop a sense of responsibility to the patient and become a member of the healthcare team (Marriner Tomey & Alligood, 2002).

Wren (2001) conducted a qualitative case study with five expert nurse anesthetists to understand and describe the learning processes of expert CRNAs. Expert nurse anesthetists were defined as those having current certification, participated in activities to upgrade skills, have 5 years experience, and identified by peer and supervisors as experts. Data collection was performed through interviews, observations, and document reviews. Validity was demonstrated through data checks with participants, peer review, and methodological triangulation. Reliability was documented through an audit trail. Three stages of learning were identified: (1) seeking of basic information, (2) continued practice, and (3) development of confidence, comfort, and finesse (Wren, 2001). This study exemplifies how CRNAs progress through the stages of skills acquisition not only as a new CRNA, but also when confronted with new situations, agents, techniques, or changes in practice. The novice and advanced beginner CRNA seeks the information from the core sciences and uses these as the "rules" or the framework that guides the practice until experience can contribute.

The second step, continued practice, is comparable to the development of the competent nurse from Benner's model in which the acquired knowledge is put into clinical practice. The CRNA is able to consistently and predictably put the information into clinical practice, and learn from the situation and experience of others. "Experience is what promotes a complete, working understanding of the basic principles" (Wren, 2001, p. 275). Assimilating knowledge gained by experience and making judgments based upon the results helps the CRNA progress to the level of proficient. Through continued practice and the use of acquired knowledge, utilizing scientific principles and experience, the CRNA develops confidence, comfort and finesse. Finesse is described as intuitively knowing what needs to be done (Wren, 2001). Achieving this third step, finesse, is comparable to reaching the stage of expert nurse from Benner's model.

Summary

The incidence of postoperative nausea and vomiting remains at about 30% despite increased understanding of etiology and treatment. Patient characteristics, anesthetic factors, and specific surgical technigues are associated with increased risk. Because the individual variations in factors that increase risk of development of PONV a varying approach to the prophylactic treatment of PONV is required. A pocket guide that outlines screening criteria and contains an algorithm based upon identified risk is helpful to practitioners entering the nurse anesthesia field.

Until the CRNA develops a wealth of experience based knowledge, a level of trust in their personal intuition, an internal "knowing what needs to be done" through subtle clues that cannot be defined, and eventually finesse, guides to help with decision-making can be instrumental. Therefore a pocket guide to assist the novice, advanced beginner, and competent CRNA in rapid and consistent screening of risk identification and determination of appropriate interventions to the determined risk is beneficial because nurses in theses stages rely on rules and are task oriented. They can minimize unnecessary suffering on behalf of the patient, facilitate decision-making, and provide care in a cost efficient method while minimizing risk of adverse effect from medications.

CHAPTER II

REVIEW OF LITERATURE

The incidence of postoperative nausea and vomiting for all patient populations and all surgeries is estimated to be about 25-30%, with intractable vomiting occurring in approximately 0.18% of all surgeries (Kovac, 2000). Despite advances in antiemetic pharmaceutical interventions, the rate of PONV has remained fairly constant over the last couple of decades. The cause of nausea and vomiting is multifactorial with the exact pathophysiology unknown. In this chapter, I will review the anatomy and physiology of the chemoreceptor trigger zone and the vomiting center. I will review the literature on the identification of risk for the development of PONV and available screening tools. I will provide information on the various antiemetics that are available and review information regarding efficacy.

Chemoreceptor Trigger Zone

The chemoreceptor trigger zone (CTZ) is a group of cells located in the postrema on the floor of the fourth ventricle in the medulla. The CTZ contains receptors for opiates, dopamine (D_2), serotonin ($5\text{-}HT_3$), histamine, and muscarinic acetylcholine. The CTZ also receives input from the vestibular portion of the eighth cranial nerve (Barash, Cullen, & Stoelting, 2001). When these receptors are stimulate by drugs, electrolytes, or metabolites, the CTZ sends signals to the vomiting center (Barash, et al., 2001). The vomiting center, which is located in the lateral reticular formation of the medulla, is responsible for controlling and coordinating nausea and vomiting. The vomiting center also receives afferent input via the vagus nerve from the gastrointestinal tract and the nucleus solitarius, which involves the gag reflex (Yuill & Gwinnutt, 2003). The CTZ is believed to have a major effect on the vomiting center. Current antiemetic drug therapy focuses on blockade of one of these receptor systems.

Risk Factors

While the cost to health care institutions for PONV can be significant, treating all patients prophylactically is not a cost effective alternative and may place patients at risk from unwanted side effects. Therefore, creation and utilization of a risk assessment tool can be helpful for screening patients at risk for developing PONV and guide treatment to prevent its occurrence. Koivuranta, Laara, Snare, and Alahuhta (1997) conducted an interview based survey of 1,107 patients, age 4 to 86, that underwent one of 16 common types of surgery. They recorded the incidence, intensity, and antiemetic needs of the patients for a 24-hour period. The purpose was to determine characteristics of patients at increased risk for PONV in order to create a risk assessment tool. Overall, 52% (n=575 of 1107) of patients developed nausea and 25% (n=277 of 1107) had emesis. The incidence of PONV was evaluated at two time intervals: 0 to 2 hours postoperatively and 2 to 24 hours postoperatively. Patients who underwent gynecologic procedures had the highest incidence of nausea and vomiting; with 27% (n=242) experiencing PONV during the immediate postoperative period and 60% (n=242) during the 24 hour period. Of those gynecological patients with nausea, 31% (n=242) also had vomiting episodes. Of all surgical procedure categories, the overall highest incidence of nausea occurred with the laparotomy gynecological patients (73%, n=102). Females (n=730) had more frequent episodes of nausea or vomiting (57% and 29% respectively) as compared to males (n=377, 32% and 12% respectively). After determining the incidence of nausea and vomiting, logistic modeling was performed to stratify risk scores. Koivuranta et al. (1997), determined a logistic coefficient for the five strongest predictors; female gender has a risk coefficient of +0.93, previous history of PONV (+0.82), duration of surgery greater than 60 minutes (+0.75) , nonsmoking (+0.61), and history of motion sickness (+0.59).. For each risk factor the patient has, the corresponding coefficients are added together to determine a risk score. A higher the score denotes increasing risk for PONV. In an attempt to simplify the score they weighted each of the five main predictors the same and found the simplified score did not loose any discriminating power (Koivuranta et al., 1997).

Identification of the factors that place a patient at risk for PONV is essential in order to adequately plan and provide prevention interventions. Risk stratification tools have been developed to aid in determining patients at risk for PONV. Apfel, Laara, Koivuranta, Greim, and Roewer (1999) studied 2,722 patients to compare risk assessment tools developed by two separate institutions to determine if the risk scores where valid across the institutions. They also investigated if the existing risk scores, which are based upon the logistic regression coefficients, could be simplified and still retain their predictive power. Using logistic regression models from prospectively collected data, they calculated an area under the curve (AUC), which represented predictive value. A score of 1.0 represented perfect discriminating value and 0.5 represented no discriminating value. Risk scores from one center were able to predict PONV from the other center with an AUC of 0.65-0.75. When they simplified the risk stratification by merely counting the presence or absence of risk factors and then determining risk, the power was not weakened (AUC of 0.63-0.73). Each major factor was applied individually to a logistical regression model, with a significance level of $p<0.05$ and the predictive value for the major factors were determined. From this process, four major predictors were identified: female gender, history of motion sickness or postoperative nausea and vomiting, nonsmoking, and use of postoperative opioids. Using the simplified risk model the above factors are identified and counted: for each risk factor the patient possesses the incidence of PONV increases. If the patient has no risk factors, there is still a 10% chance of PONV, 1 risk factor is associated with a 21% chance, 2 risk factors a 39% chance, 3 risk factors a 61% chance, and all 4 risk factor confers a 79% chance of PONV (Apfel et al., 1999).

Sinclair, Chung, and Mezei (1999) performed a large prospective study of 17,638 consecutive patients having outpatient surgery during a three year period to characterize the incidence rate of PONV and to determine predictive factors. After completion of descriptive statistics, the researchers completed a logistic regression with backward stepwise elimination to develop a predictive model. To validate the model the patient sample was divided into two groups; one half the sample was for model development and the other half then had predictive scores calculated and was used to validate the model. Age, sex, smoking status, previous PONV, type of anesthesia, duration of anesthesia, and type of surgery were independent predictors for PONV. Every 10 year increase in age greater than 50 years decreases the likelihood by 13%, {Odds Ratio (OR)=0.87, 95% Confidence Interval (CI) 0.8-0.9, P=0.0008}. Men had one third the risk of PONV of women (OR=0.36, 95% CI 0.3-0.5 P=0.0001). Smokers had two-thirds the risk for

PONV than nonsmokers (OR=0.66, 95% CI 0.5-0.9, P=0.13). Patients with a previous history of PONV had three times the risk of developing PONV with subsequent surgeries (OR=3.13, 95% CI 2.1-4.6, P=0.0001). General anesthesia with a volatile agent had the strongest predictive value with a 10.6 (95% CI 6.7-16.7, P=0.0001) when compared to monitored anesthesia care, regional, or chronic pain block. There was a direct association between duration of surgery and PONV, with every 30 minute increasing the risk by 59% (OR=1.59, 95% CI 1.4-1.8, P=0.0001). Certain surgeries were associated with increased risk for development of PONV by a six fold factor: plastic (OR=6.68, 95% CI 3.5-12.6, P=0.0001), strabismus (OR=5.85, 95% CI 3.8-9.0, P=0.0001) and orthopedic shoulder surgeries (OR=5.91, 95% CI3.4-10.3, P=0.0001). ENT surgeries were associated with a 4 fold increase in PONV, while non dilation and curettage gynecological (OR=3.31, 95% CI 2.3-4.8, P=0.0001) and non-shoulder orthopedic surgeries (OR=2.57, 95% CI 1.4-5.5, P=0.0006) indicated a three fold increase (Sinclair et al., 1999). While the mathematical model developed proved to accurately predict PONV, the model is cumbersome and requires the assistance of a calculator to determine a predictive value, therefore limiting its use at the patient bedside as a rapid screening tool.

In recent years many studies have been performed to determine risk factors associated with PONV. Habib and Gan (2004) performed a review of the literature from randomized controlled trials, systemic reviews, logistic regressions analyses, and expert opinion to rank the level and strength of the evidence. From this process they developed an evidence-based guideline for the prophylaxis and treatment of PONV. The risk factors in their guide are from one of three categories: anesthetics factors, patient factors, and surgical factors. The anesthetic risk factors of PONV were determined by systematic review and include volatile agents, nitrous oxide, opioids both by intraoperative and postoperative, and high doses of neostigmine. Female gender is a patient-related risk factor that has been supported in large, randomized controlled trials. Such trials provide good evidence to support a conclusion regarding the gender risk. Other patient related risk factors include history of PONV or motion sickness and nonsmoking status have good support as determined by non-randomized, controlled trials and case studies. Long surgical procedures, with each duration increase of 30 minutes increasing the PONV risk by 60%, provided good evidence of support from non-random, controlled trials. The review found fair evidence to support a conclusion of increased PONV risk in association with certain types of procedures such as intra-abdominal, major gynecological, laparoscopic, breast, ENT, and strabismus (Habib & Gan, 2004).

To evaluate the relationship between pain, the dosage of morphine, and the incidence of postoperative emesis Chia, Kuo, Liu, Sue, Hsieh, and Chow (2002) performed a prospective, controlled study of 625 subjects undergoing gynecological surgery. Since multiple factors influence the development of PONV, the study population was carefully selected to exclude patients with significant risk factors in an attempt to minimize extraneous variables. Patients with a history of PONV, motion sickness, drug abuse, and smoking, as well as those menstruating or under hormonal therapy were excluded. Also patients allergic to morphine, and patients with underlying cardiovascular, respiratory, liver, and kidney disease were excluded. Anesthetic technique was consistently applied for all subjects in the study. Postoperative pain was treated with patient controlled analgesia, which was programmed the same for all subjects. Patients rated their pain using visual analog scales at rest and with movement.

The subject population was grouped according to outcome, those with emesis and those without, to evaluate the differences in pain level, opiate usage, and incidence of emesis. There was no statistical difference between demographics in each group. For three days following the surgical procedure the patients were assessed for occurrence of emesis, sedation, pain intensity, and amount of morphine used. The incidence of emesis for days 1, 2, and 3 were 26%, 13%, and 4% respectively. Visual analog scores were significantly different both at rest and with movement between the two groups with $p < 0.05$. Morphine consumption was not significantly different except for those patients with emesis on day 3. To avoid covariant bias, logistic regression analysis was performed and determined that pain intensity with cough or movement was a more sensitive factor to predict postoperative emesis. The authors determined that postoperative pain may be a factor in increasing the incidence of emesis in patients undergoing general anesthesia for major gynecological surgery.

Risk Profiling

Several risk factors have been identified and six predictive tools have been developed to determine the risk of PONV. Although predictive tools have been developed, few studies have been conducted to test the validity and practicability of these models. Four of these models allow for the calculation of an actual score that correlates with risk and the other two models classify patients as high risk or low risk, having a 30% chance of PONV as the classification level. Apfel, Kranke, Eberhart, Roos, and Roewer (2002) conducted a study of 1,566 subjects having balanced general anesthesia without antiemetics treatment to compare the discriminating power, calibration characteristics, and practicability of these six models. Following surgery the subjects were assessed at three different time intervals for any patient report of nausea or emetic episode: before leaving the PACU, at least 6 hours postoperatively, and the following day (at least 24 hours postoperatively). In the study, the incidence of PONV was 38.3% (n=1,566). Each subject was evaluated utilizing all six risk models. This resulted in four probability scores, one from each model that enables score calculations, or classified as high or low risk according to the other two models. Each probability or classification was used to create a receiver operating characteristic (ROC) curve. The ROC curve displays the correlation between the specificity and sensitivity for all possible values of probability that an event is expected to occur. "Therefore, the area under the ROC curve (AUC) is an overall measure of a risk score/model to discriminate patients with PONV from those without PONV (discriminating power) and is frequently used to compare different risk scores" (Apfel et al., 2002, p. 235).

The researchers compared the AUCs of the different models in three ways. First, the AUC was calculated by the original models. Three models were determined to have significantly higher discriminating power as determined by AUC; these are listed by first authors' name: (a) Apfel (1999), AUC 0.68, 95% CI 0.66-0.71; (b) Koivuranta (1997) AUC 0.70, 95% CI 0.67-0.72; and (c) Sinclair (1999) AUC 0.68, 95% CI 0.66-0.71, as compared to the scores of (d) Palazzo (1993) AUC 0.64, 95% CI 0.62-0.67; (e) Gan (2000) AUC 0.61, 95% CI 0.58-0.63; and (f) Scholz (2000) AUC 0.61, 95% CI 0.58-0.63 ($P<0.05$).

Secondly, the four models that allow calculation of scores were divided in risk class of low risk, mild to moderate risk, high risk, and extremely high risk. The risk categories were developed so that all scores had the same number of decision criteria and surgery. Using the predictive model created by Apfel and collogues (1999); patients were screened for the presence of the four risk factors: female gender, history of PONV or motion sickness, nonsmoking status, and anticipated use of postoperative opioids. Patients were classified as low risk if they have 0-1 risk factors and high risk if 2 or more risk factors. High risk patients prophylactically received 4 mg of ondansetron 30 minutes before the end of surgery and low risk patients received rescue ondansetron treatment if needed. There was no significant difference between group's anesthetic techniques, surgical procedures, duration of surgery, and time in the PACU. Forty-four patients were classified into the low risk with an anticipated PONV rate of 20.5% or nine patients. The high risk group, with patients having two or more risk factors, contained 115 patients with anticipated PONV rate of 57.4% or 66 patients. The overall institutional PONV incidence was 36.5% (n=159) with 9 patients (20.5%) in the low risk group (n=44) and 49 patients (42.6%) from the high risk group (n=115) developing PONV. The incidence of PONV in the high risk group was significantly lower following prophylactic treatment than was expected ($P<0.05$). What concerned the researcher was the incidence of PONV was twice that in the low risk group. Two possible explanations included that the use of a dichotomous classification may miss the highest risk patients and use of single agent in that patient population may might be adequate and a multimodal approach based upon anticipated risk may lower the incidence of PONV (Biedler et al., 2004).

Antiemetic Agents

The chemoreceptor trigger zone serves as a sensor and is stimulated by drugs, electrolytes, and metabolites. When these receptors are activated impulses are relayed to the vomiting center, initiating the vomiting reflex. The CTZ contains receptors for cholinergics, serotonergic, dopamergic, histaminic, and opioid receptors. Mechanism of action of the commonly used antiemetics involves blockage of these neurochemical receptors sites (Kovac, 2000).

Anticholinergics

"The anticholinergics are potent inhibitors of muscarinic and cholinergic CNS receptors in the cerebral cortex and pons (Kovac, 2000 p. 220)." This is the oldest class of antiemetic agents. Atropine and scopolamine, which are tertiary amines, readily cross the blood brain barrier and effect the M3 and M5 muscarinic receptors, these receptors selectively possess activity against motion sickness (Kovac, 2000).. These agents are most efficacious against motion sickness. Transdermal scopolamine in the most potent and efficacious drug anticholinergic to be used as an antiemetic and is especially effective at preventing opioid induced PONV (Kovac, 2000). The transdermal patch should be applied the evening prior or four hours prior to the conclusion of surgery (Habib & Gan, 2004). The most commonly reported side effects for this class of drugs include: dry mouth, sedation, visual disturbances, mydriasis, memory loss, urinary retention, hallucinations, confusion, and disorientation. Anticholinergics are contraindicated in closed angle glaucoma (Yuill & Gwinnutt, 2003).

Scopolamine in combination with ondansetron decreased the incidence of nausea following general surgery compared to placebo (Jones, Strobl, Crosby, Burkard, Maye, &.Pellegrini, 2006). In a randomized, double-blind placebo controlled study of 56 patients; Jones et al. (2006) evaluated the effects of scopolamine patch applied within two hours of surgery on subjects having a variety of surgery lasting longer than 60 minutes. All patients received ondansetron at the end of surgery, patients were randomized to have a scopolamine patch or placebo patch applied. All patients were screened using Koivuranta's (1997) simplified method and required to have at least three risk factors. Subjects who received placebo reported an incidence rate during the first 24 hours of 75% (n=21 of 28) compared to scopolamine only 39% (n=11 of 28) (P=0.007) (Jones et al., 2006). Antiemetic therapy was also required more frequently in subjects who received placebo compared to scopolamine (P=0.007) (Jones et al., 2006). Combination therapy with scopolamine and ondansetron is effective at decreasing the incidence of nausea and failed prophylaxis of nausea in high risk patients compared to monotherapy with ondansetron.

Dopamine Receptor Antagonists

Several drugs have been shown to antagonize the dopamine (D2) receptors in the CTZ. The antiemetic medications in this group include the phenothiazines, benzamides, and butyrophenones. The phenothiazines have a direct antagonistic effect on the D2 receptors in the CTZ. They also have moderate antihistaminic and anticholinergic activities. These medications are sometimes used as sedatives and major tranquilizers. The phenothiazines antiemetic effects are most effective at counteracting the effects of certain drugs, especially opioids, on the CTZ (Kovac, 2000). The phenothiazines are less effective against motion sickness and have no effect on gastric emptying. Perphanazine, a heterocyclic phenothiazine, has been shown to decrease the frequency of vomiting after tonsillectomy in children. Splinter and Roberts (1997) performed a randomized, double-blind study of 260 children age 2-12 undergoing elective tonsillectomy. The patients were randomized to receive either perphanazine 70 micrograms per kilogram, maximum dose of 5 mg, or placebo before surgery. Both groups were determined to be statistically similar. In the 24 hours following surgery, those patients who received perphenazine had a 42% incidence of vomiting (n=128) while the incidence of vomiting following placebo was 57% (n=130). There was a significant decrease in vomiting following the administration of perphenazine versus placebo (P<0.01). The patients who received prophylactic treatment with perphenazine required a significantly less rescue antiemetics than those who received placebo (p<0.05). Prophylactic administration of perphanazine decreases vomiting following tonsillectomy (Splinter & Roberts, 1997). The phenothiazines have been shown to be effective antiemetics; however, they have an extensive adverse profile. The phenothiazines cause sedation and hypotension. Extrapyramidol side effects especially following administration with higher doses and prolonged use and are more common with perphanazine and prochlorperazine than the other phenothiazines (Yuill & Gwinnutt, 2003). Neuroleptic malignant syndrome which involves catatonia, autonomic instability, hyperthermia, muscle rigidity, and myoglobinemia, has been reported with phenothiazines (Kovac, 2000).

The butyrophenones, haloperidol and droperidol, are strong dopamineric receptor blockers in the CTZ and are postrema. They are also alpha-blockers, which are associated with sedation and extrapyramidol side effects. Butyrophenones, in repeated high doses, are also associated with anxiety, restlessness, and hypotension. Both haloperidol and droperidol have been shown to be effective antiemetics; however droperidol in more commonly used in anesthesia (Kovac, 2000). Droperidol's antiemetic properties have duration of action as long as 24 hours, this is believed to occur because of the high affinity and longer binding time of droperidol to the D2 receptors in the CTZ (Kovac, 2000). Droperidol in small doses of 0.625 mg was found to be as effective as

1.25 mg intravenously for the prevention of PONV (Kovac, 2000). In December 2001, the Federal Drug Administration (FDA) issued a black box warning on the use of droperidol. A black box warning is the most serious warning issued for an FDA approved drug. Droperidol was found to be associated with QT prolongation and/or torsades de points and was associated with fatal cardiac dysrhythmias (Habib & Gan, 2004).

The prolongation of QT interval and cardiac dysrhythmias were associated with high doses of droperidol, no studies have been conducted to evaluate the effects of anesthetic doses of droperidol on the QT interval. White, Song, Abrao, Klein, and Navarette (2005) conducted a randomized, double-blind, placebo controlled study of subjects undergoing general anesthesia for otolaryngeal procedures to evaluate the effects of low dose droperidol on the QT interval. After standard induction of general anesthesia 60 subjects were randomized to one of three treatment strategies; saline(control), droperidol 0.625 mg, or droperidol 1.25 mg, all placed in numbered identical two milliliter syringes. Electrocardiogram was continuously recorded in Lead II for 2-3 minutes prior to injection and for 10 minutes after injection. The QT interval corrected for heart rate (QTc) was calculated every minute throughout the continuous recording. The QTc was prolonged in all three groups at three to six minutes after injection and no statistically significant difference was found in the mean maximum prolongation between groups (White et al., 2005). However, two patients in the droperidol group experienced QT prolongation for longer than 60 seconds and one patient who received droperidol 0.125 mg developed QT prolongation of greater than 133 milliseconds (White et al., 2005). Small dose droperidol, 0.625 or 1.25 mg, was not associated with any significant prolongation of the QT interval; however, the sample size was to small to make any definitive conclusions.

The benzamides, metoclopramide and domperidone, are specific D2 dopamine receptor antagonists. Metoclopramide blocks dopamine receptor centrally in the CTZ and peripherally in the gastrointestinal tract. Gastrointestinal motility is increased and the lower esophageal sphincter tone is increased this acts to prevent the delayed gastric emptying frequently encountered with opioid use. "The efficacy of metoclopramide in preventing PONV… is uncertain, with approximately 50% of the studies showing it to be no more effective than placebo" (Habib & Gan, 2004, p. 330). The adverse effect of metoclopramide are relatively few and do not effect hemodynamic stability or sedation post anesthesia, however it has been associated with extrapyrimidol side effects (Kovac, 2000). Habib and Gan (2004) stated that the majority of members of the consensus panel felt Metoclopramide could not be recommended as an antiemetic. Metoclopramide is probably best utilized preoperatively for known or suspected delayed gastric emptying or gastroesophageal reflux (Yuill & Gwinnutt, 2003). Domperidone, like Metoclopramide, acts both centerally in the CTZ and has prokinetic effects in the gastrointestinal tract promoting GI motility and increasing lower esophageal sphincter tone. Domperidone appears to be more efficacious against active PONV (Kovac, 2000). Since domperidone does not cross the blood-brain barrier, sedation and the occurrence of extrapyramidol side effects are lessened (Yuill & Gwinnutt, 2003). Cardiac arrhythmias have been noted with large doses of domperidone (Yuill &Gwinnutt, 2003).

Antihistamines

The antihistamines exert their activity directly in the vomiting center and the vestibular tract. These medications are most effective in the treatment of motion sickness and vertigo. The antihistamines, dimenhydrinate, diphenhydramine, cyclizine, and hydroxyzine, act by blocking acetylcholine in the vestibular apparatus and blocking the histamine (H1) receptors in the nucleus of the solitary tract (Kovac, 2000). The antihistamines are "the drugs of choice to control PONV following operations on the middle ear" (Kovac, 2000, p. 225). The major side effects include sedation, dry mouth, blurred vision, urinary retention, and prolonged recovery times (Kovac, 2000). Cyclizine is frequently used in the United Kingdom, but is contraindicated in acute myocardial infarction because is aggravates heart failure and may also counteract the beneficial effects of the opioids (Yuill & Gwinnutt, 2003).

Serotonin Receptor Antagonists

The serotonin (5-HT3) receptor is highly specific for nausea and vomiting and the CTZ contains a high concentration of these receptors. The 5-HT3 receptor antagonist binds to receptors in the CTZ and at vagal afferent receptor in the gastrointestinal tract. The limited side effect profile makes this class of drug an ideal option especially for ambulatory surgery (Habib & Gan, 2004). The side effects of the 5-HT3 receptor antagonists include headache, most commonly, dizziness, flushing, elevated liver enzymes, and constipation (Habib & Gan, 2004).

Ondansetron was the first serotonin receptor antagonist approved for PONV in both adults and children. "The optimal effective dose was found to be 8 mg orally administered 1 to 2 hours before anesthesia or 4 mg intravenously at the start of anesthesia" (Kovac, 2000, p. 227). Ondansetron has more effective anti-vomiting properties than anti-nausea properties (Habib & Gan, 2004). Recent studies have shown the odansetron given at the end of surgery is more efficacious than at the beginning. While the manufacturer of ondansetron recommends PONV prophylactic be given before induction, it has been shown that odansetron 4 mg intravenous administered at the end of surgery is more efficacious at preventing PONV in the immediate recovery period and for 24 hours following surgery (Tang et al., 1998).

Tang et al. (1998) performed a randomized, double-blind, placebo controlled study of 164 women undergoing outpatient laparoscopic gynecological procedures to determine the effect of timing of ondansetron administration on the severity, incidence and costs associated with PONV. Discharge characteristic, patient satisfaction, and patients willingness to pay for antiemetics were also compared. The subjects were randomly assigned to one of four groups, Group A received placebo of saline before induction and at the end of surgery, Group B received ondansetron 2 mg at induction and 2mg at the conclusion of surgery, Group C received ondansetron 4 mg at the induction of surgery and saline at the conclusion of surgery, and Group D received saline at induction and ondansetron 4 mg at the end of surgery. Demographic data, anesthetic management, anesthesia time, and surgical time were not statistically different between groups. Regardless of the timing of administration, both groups that received ondansetron 4 mg in a single dose experienced significantly less nausea than placebo ($P<0.05$) and Group D had significantly less vomiting than placebo ($P<0.05$) in the postanesthesia recovery area. During the first 24 hours postoperatively, the subjects administered ondansetron at the end of surgery had significantly lower nausea scores than all the other groups and experienced fewer vomiting episodes than those who received placebo or ondansetron at the beginning of surgery (P<0.05). The time from the end of anesthesia until 25% of the group failed prophylactic treatment was significantly less in the subjects who received ondansetron at the end of surgery compared to all other groups (P<0.05) with >1440 minutes in Group D (Tang et al., 1998). The researchers concluded ondansetron at the end of surgery is more effective at preventing PONV in the postanesthesia care unit and 24 hours following surgery. And ondansetron either at the beginning or end of surgery is more efficacious than placebo at reducing the incidence of nausea in the immediate recovery period.

In various studies "there is no evidence of any difference in efficacy or side-effect profile between the various 5-HT3 receptor antagonists, when appropriate doses are used"(Habib & Gan, 2004, p. 329). The optimal effective dose of granisetron is 1 mg at the beginning of surgery (Kovac, 2000). Strong evidence exists to support the granisetron dose of 0.1mg to be effective for the treatment of existing PONV (Habib & Gan, 2004). Tropisetron has an elimination half-life of 8 to 12 hours and the effective prophylactic dose is 2 to 5 mg with the majority of studies of this drug being conducted in Europe (Habib & Gan, 2004). Dolansetron is the only 5-HT3 receptor antagonist that is converted to an active metabolite, hydrodolansetron, which is responsible for the majority of its antiemetic properties (Kovac, 2000). The recommended intravenous prophylactic dose is 12.5 mg administer 15 to 30 minutes prior to the end of surgery (Kovac, 2000).

Nontraditional Antiemetic Therapy

Some drugs, although not specifically designed for antiemetic use, have been shown to have properties that decrease nausea and emesis either individually, additively, or synergistically. Two common agents in the anesthetic arena, corticosteroids and propofol, will be discussed here.

Corticosteroids

Corticosteroid use as an antiemetic was first found with chemotherapy induced nausea and vomiting. The mechanism of action is believed to be anti-inflammatory and/or membrane stabilizers (Kovac, 2000). Henzi, Walder, and Tramer (2000) performed a quantitative systemic review of the literature to obtain information about the efficacy and safety of dexamethazone for the prevention of PONV after general anesthesia. Antiemetic efficacy was defined as the prevention of a PONV event with dexamethazone or control and is listed as number needed to treat (NNT). The number needed to treat is the number of patients who require treatment in order to prevent one episode of PONV that would have occurred had all subjects received a placebo or control (Henzi, et al., 2000). A positive number needed to treat represents superiority of dexamethasone over control, while a negative number represents improved efficacy of the control over dexamethasone (Henzi, et al. 2000).

Seventeen randomized controlled trials that compared dexamethazone and a comparator were analyzed. Data from these studies involved 1,961 subjects: 598 subjects received dexamethazone while 582 received ondansetron, granisetron, droperidol, metoclopramide, or perphenazine. A placebo was received by 423 subjects and 343 received a combination of dexamethasone and a 5-HT3 receptor antagonist. All studies showed a statistically significant difference when comparing dexamethasone with placebo. The data from seven studies comparing dexamethasone to placebo was combined to increase power and calculate a number needed to treat, which is an indicator of clinical efficacy. The NNT to prevent PONV in the first 6 hours following surgery, the early phase, was 7.1 (95% CI 4.5 to 18) and to prevent PONV up to the first 24 hours, the late phase, was 3.8 (95% CI 2.9-5). Two trials conducted with adults subjects analyzed the antinausea effects of dexamethasone compared to placebo, the NNT was calculated to be 4.3(95% CI 2.3-26) (Henzi et al., 2000). Compared to placebo dexamethasone has improved efficacy in late vomiting and preventing nausea.

Dexamethasone, when compared to other antiemetics, proved to be less effective. The 5-HT3 receptor antagonists had a NNT of -5.9 (95% CI -3.5to -20) for the prevention of early vomiting when compared to dexamethazone (Henzi et al., 2000). The concomitant use of dexamethazone with other antiemetics, especially when combined with a serotonin receptor antagonist (5-HT3), showed a statistically significant improvement in late nausea and vomiting with NNT of 7.8 (95% CI 4.1 to 66) and 7.7 (95% CI 4.8-19) respectively compared to5-HT3 antagonist monotherapy. When comparing the concomitant use of dexamethazone and a 5-HT3 receptor antagonist versus a placebo, the event rates were very low for nausea and vomiting in both the early and late outcomes (Henzi et al., 2000). The adverse effects were most frequently reported when dexamethazone was combined with a 5-HT3 receptor antagonist are more frequently associated with the latter. The side-effects most reported include headache, dizziness, drowsiness, and sedation, constipation, and muscle pain. No studies evaluated the effects of hypothalamic-pituitary adrenal (HPA) axis inhibition. However, in other studies utilizing 20 mg of dexamethazone per day for 5 days to control nausea and vomiting induced by chemotherapy, no evidence of immunosuppression or HPA axis dysfunction was found (Henzi et al., 2000). Dexamethazone has antiemetic properties when compared to placebo without evidence of adverse side effects and is more efficacious at preventing nausea and vomiting up to 24 hours after surgery. The combination of dexamethazone and a 5-HT3 receptor antagonist is most efficacious for prophylactic therapy of PONV.

Propofol

A sedative hypnotic agent, frequently used for the induction of anesthesia, has been associated with decreased nausea and vomiting. The exact anti-emetic of propofol is unknown (Kovac, 2000). A meta-analysis of prospective randomized studies comparing propofol with inhalational agents for incidences of nausea, vomiting, or nausea and vomiting revealed a 3.7 fold reduction in the incidence with propofol (Sneyd, Carr, Byrom, & Bilski, 1998). A comprehensive review of the MEDLEY database of Zeneca Pharmaceuticals determined 96 publications to meet the eligibility requirements as determined by independent researchers. The induction agent, maintenance agent, analgesic, presence of absence of nitrous oxide, age, type of surgery, and the number of patients with nausea, vomiting, or nausea and vomiting were recorded. A significantly lower incidence of vomiting was found among patients induced and maintained with propofol compared to inhalational agents ($P<0.0001$). The common odds ratio was estimated to be 0.267 (95% CI: 0.220, 0.325) this represents a 3.7 fold risk reduction for subjects treated with propofol compared to other agents (Sneyd et al.,1998). Type of surgery, opiate narcotic usage, patient age, and nitrous oxide did not appear to influence the odds ratios. The mean number needed to treat (NNT) was 7.1 (95% CI, 5.6-9.7): representing for every seven patients treated with propofol for induction and maintenance this would prevent PONV in one patient who would have developed PONV had they all been treated with inhalational agents (Sneyd et al., 1998).

Antiemetic Management

Of the many studies performed evaluating antiemetic therapy options and efficacy no single agent has proven to be any more effective than another. Despite numerous antiemetic choices available, the rate of PONV remains at about 30%. While combination therapy utilizing agents from different classes in combination seems the most effective, it is not cost effective for all patients and is not without potential risk from adverse effects. The existing studies conducted have compared single interventions or have not contained sufficient power to allow conclusions to be drawn. Because of the deficiency in supporting data, a consensus conference has been unable to determine a definitive statement on the benefits of combined therapy.

Different interventions have proven effective as reducing the incidence of PONV, but no therapeutic regime has shown to be 100% effective in the prevention of PONV. Scuderi, James, Harris, and Mims (2000) developed a multimodal management strategy for high risk patients that was 98% effective in the prevention of postoperative nausea and vomiting. One hundred thirty nine subjects undergoing laparoscopic gynecological procedures under general anesthesia were randomly assigned to one of three treatment groups. Group M (n=60) received a multimodal therapy: TIVA with propofol and remifentanil; avoidance of nitrous oxide and nondepolarizing neuromuscular blockers; vigorous intravenous hydration; triple antiemetic regime with ondansetron, dexamethasone, and droperidol; and Ketorolac for postoperative pain control. Group O (n=42) received a balanced anesthetic technique and antiemetic prophylaxis with ondansetron, while Group P (n=37) was administered balanced anesthesia with placebo. No subject in the multimodal treatment experienced vomiting and only one subject required treatment for nausea denoting a 98% response rate, this was statistically different than subjects in the other two groups ($P<0.0001$) (Scuderi et al., 2000).

The International Multicenter Protocol to Assess the Single and Combination Benefits of Antiemetic Interventions in a Controlled Clinical Trial (IMPACT) study, a large, multicenter clinical trial of factorial design, was conducted to evaluate the interaction among six antiemetic interventions and to determine efficacy by combining two or three interventions was undertaken by (Apfel et al., 2004). The IMPACT study enrolled 5,199 adult subjects in 28 participating centers undergoing elective surgery under general anesthesia lasting one hour or longer. The primary outcome evaluated was nausea and vomiting within 24 hours after surgery. All patients included in the study were to possess at least two of the following risk factors which confers to a 40% or greater chance of PONV: female gender, nonsmoking status, history of PONV or motion sickness, and anticipated need for postoperative opiates. The six intervention evaluated involved three antiemetics; ondansetron, dexamethasone, and droperidol, and three anesthetic techniques; total intravenous anesthesia (TIVA) with propofol instead of volatile agent, the use of nitrous oxide, and remifentanil versus fentanyl. Combination of these six different interventions allows for 64 treatment options using a 2x2x2x2x2x2 factorial design. To ensure sufficient power of the effects of propofol in combination with antiemetics twice as many patients were assigned to receive TIVA versus volatile agents. The patients in each center were randomized to receive one of four treatment options that were stored in a randomized sequentially numbered sealed envelope.

Overall, 34% (n=1731 of 5161) of patients developed postoperative nausea and vomiting. The highest incidence of PONV, 59% (n= 26 of 44), occurred in the treatment group who received volatile agents, nitrous oxide, Fentanyl, and no antiemetics. While the lowest incidence, 17% (n=17 of 102), occurred in the patients who were treated with propofol, nitrogen, remifentanil, ondansetron, dexamethasone, and droperidol. Utilizing bivariant analysis, each antiemetic reduced the incidence of PONV by about 26%, use of propofol reduced the incidence by about 19%, and use of nitrogen instead of nitrous oxide reduce PONV by about 12% (Apfel et al., 2004). By increasing the number of antiemetics administered, there is a corresponding risk reduction of 26% (n=5,161) for each additional antiemetic, the incidence of PONV was 52% (n=5,161) when no antiemetics were used, 37% (n=5,161) with one antiemetic, 28% (n=5,161)with two antiemetics used, and 22% (n=5,161)when three antiemetic were administered (Apfel et al., 2004). No antiemetic tested was significantly better than any other antiemetics (P=1.0) and no combination better than any other combination (P=0.81) (Apfel et al., 2004). The use of remifentanil did not significantly reduce the risk of PONV as compared to the use of Fentanyl (P=0.21) (Apfel et al., 2004).

Using this information the researchers calculated an estimated incidence of postoperative nausea and vomiting as determined by the relative baseline risk of each patient, assuming that each intervention reduces the risk by 26%. For example, a patient with an 80% baseline risk of developing PONV would to have their risk reduced to 59% by utilizing one intervention and 24% by employing four interventions. In contrast the patient with only a 10% baseline risk would have the risk reduced to 7% with one intervention and decreased to 3% with using all four interventions (Apfel et al., 2004). This supports the concept that prophylactic strategies should be adjusted according to baseline risk with the maximum benefit of additional interventions being provided to patients whose baseline risk is greatest.

Regional Anesthesia

Regional anesthesia is generally considered to result in a lower incidence of PONV in part because the technique allows avoidance of several agents known to be emetogenic, particularly volatile agents and nitrous oxide. Few studies on regional anesthesia have been conducted to investigate PONV, and when reported are usually considered as part of the secondary outcome analysis. The incidence of PONV associated with regional anesthesia is estimated to be 25% and vary according to type of surgical procedures, additives to the local anesthetics, and medical sequela from the regional such as hypotension (Borgeat, Ekatodramis, & Schenker, 2003). Hypotension associated with neuraxial anesthesia is implicated in increased frequency of PONV; this is thought to be secondary to brain stem ischemia and activation of the circulatory, respiratory and vomiting centers (Borgeat et al., 2003). Supplemental oxygen and adequate hydration are beneficial in relieving nausea related to hypotension (Borgeat et al., 2003).

The incidence of PONV with subarachnoid block varies widely with intraoperative rates of nausea being 18% with vomiting occurring in approximately 7% of patients (Borgeat et al., 2003) Major orthopedic procedures and caesarian sections have repeated been associated with high rates of PONV (Borgeat et al., 2003). Incidence of

PONV is not affected by the local anesthetic agent or dosage, however adjunctive medications added have varying effects on PONV. Epinephrine has been shown to be emetogenic when given subarachnoid even without differences in hypotension; its effects may be related to increased serotonin release and direct activation of the alpha-adrenergic receptors in the CTZ (Borgeat et al., 2003). Subarachnoid opioid effects on nausea and vomiting are related to the agent used, meperidine has the highest incidence of PONV and should be avoided, morphine is emetogenic in a dose dependant effect but does not seem to increase risk when given with major surgeries, while fentanyl and sufentanil are lowest risk for inducing nausea or vomiting (Borgeat et al., 2003).

Epidural anesthesia has varying reports in the incidence of PONV but the use of local anesthetic alone is associated with very low risk (Borgeat et al., 2003). Addition of morphine to the epidural has been implicated to increase risk of PONV development while the other opioids have not, fentanyl or sufentanil carry the lowest risk and should be used in place of morphine (Borgeat et al., 2003). Epinephrine in epidural anesthesia is not associated with increase PONV; however, its clinical use in the situation is not recommended (Borgeat et al., 2003). The use of peripheral nerve blocks is favorable for the prevention of PONV with incidence reported to be 4.3% to 8.8% (Borgeat et al., 2003). The use of opioids as adjuncts in peripheral nerve block is controversial and their potential to cause PONV should be considered when planning anesthetic regime (Borgeat et al., 2003). Overall, regional anesthesia is proven to decrease the risk of PONV when planning anesthetic strategy to decrease the risk of PONV adjunctive medication use benefits and risks should be considered.

Prophylactic Strategy

A multidisciplinary panel of experts convened to review the medical literature on PONV and to produce guidelines for its management (Gan et al., 2003). The goals for this guideline were to: (a) identify the primary risk factors for PONV in adults and children; (b) reduce the baseline risks; (c) identify the optimal approach to PONV prevention and therapy, to determine the optimal choice and timing of antiemetic administration; and (d) to identify the most effective therapy regimes, either monotherapy or combination (Gan et al., 2003).

The panel agreed that prophylactic treatment should be reserved for patients with moderate to high risk and those who the risk of vomiting may be associated with morbidity (Gan et al., 2003). The first part of guideline, or Guideline 1, involves identification of adults at high risk for PONV. The risk factors identified include patient, surgical, and anesthetic related factors. The patient factors are female gender, nonsmoking status, and history of PONV or motion sickness. Anesthetic factors involve the use of volatile anesthetics, use of nitrous oxide, and use of intraoperative and postoperative opioids. Duration of surgery with each increase of 30 minutes increasing the risk by 60% is a surgical related factor (Gan et al., 2003). An example of this would by a surgical procedure of 45 minutes duration and patient's baseline risk of 30% would increase the risk to 48% for development of PONV. There is fair evidence to support that certain surgical procedures increase risk with laparoscopy, ear-nose-throat, neurosurgery, breast, strabismus, laparotomy, and plastic surgery with increased risk (Gan et al., 2003).

Guideline 2 focuses on identifying children at risk for the development of PONV. The risk factors for children are the same as for adults except for a few important differences. The incidence of vomiting in children is twice as frequent as adults (Gan et al. 2003).Characteristics that determine high risk for postoperative vomiting (POV) in children include age with the incidence highest in children older than 3 years of age through puberty, the incidence tapers when a child reaches puberty (Gan et al., 2003). The gender differences are not seen with children (Gan et al., 2003). Surgical procedures associated with increased risk include tonsillectomy and adenoidectomy, strabismus repair, hernia repair, orchipexy, and penile surgery (Gan et al., 2003).

Guideline 3 involves reduction of baseline risk when able. The following recommendations have good evidence to reduce the risk of PONV: use of regional anesthetic when applicable, use a TIVA approach with propofol, use of hydration, avoiding the use of nitrous oxide, avoiding volatile anesthetics, minimizing the dosage of intraoperative and postoperative opioid, minimization of neostigmine, and non-pharmacological therapies (Gan et al., 2003). Fair evidence to support the reduction of PONV is provided for the use of supplemental oxygen intraoperatively (Gan et al., 2003). Providing adequate hydration and even super hydration with increased volumes of hydration up to 30 milliliters per kilogram decreases the incidence of nausea and vomiting (P=0.001) (Goodarzi, Matar, Shafa, Townsend, & Gonzalez, 2006). Providing super hydration is an inexpensive addition to the prevention of PONV. Data on the significance of neostigmine's effect on PONV inconclusive, Cheng, Sessler, and Apfel (2005) determined it was not emetogenic in contradiction of previous research. Until more conclusive evidence exists minimization of the use of neostigmine remains warranted.

Consensus guideline for prophylactic treatment involves a stepwise approach, first determine the level of risk (low, moderate, or high) as this will guide prophylactic therapy (Gan et al., 2003). Prophylactic treatment is not recommended for patient with low baseline risk unless medical sequela is expected to develop with vomiting (Gan et al., 2003) . Regional anesthetic should be considered for all patients with moderate to high risk (Gan et al., 2003). If general anesthesia is to be used, strategies to minimize risk should be employed as suggested in Guideline 3 (Gan et al., 2003). For moderate risk patients, prophylaxis involves monotherapy; a 5-HT3 receptor antagonist, dexamethasone, or droperidol, are all considered acceptable first line therapy. Combination therapy, which has a response rate of 98%, has been shown to be superior to monotherapy for prophylaxis (Scuderi et al, 2000). In combination therapy, medications with different mechanisms of action should be used to maximize efficacy (Gan et al, 2003). For high risk patients, strategies to be implemented include interventions to decrease baseline risk and combination therapy with two or three agents from different classes (Gan et al., 2003). Optimal antiemetic dosing with combination therapy needs to be established (Gan et al., 2003).

When PONV develops following surgery, treatment choices are guided based upon if prophylaxis was given, which agent was used, and the time interval when PONV develops. If the patient has not received prophylaxis or has received dexamethasone monotherapy, a small dose of a 5-HT3 receptor antagonist should be used at the first sign of PONV (Gan et al., 2003). Small dose therapy generally means one-fourth the standard dose. When prophylaxis with a 5-HT3 antagonist fails to prevent PONV, the patient should be treated with a drug from another class such as droperidol or promethazine (Gan et al., 2003). Triple therapy dosing regime has never been tested. If prophylaxis fails 6 hours or more after surgery a dose of the 5-HT3 antagonist or droperidol may be repeated (Gan et al., 2003). Dexamethasone dosing should not be repeated more than every 8 hours (Gan et al., 2003).

Summary

Several factors have been implicating with increasing risk for the development of PONV, these include patient characteristics, anesthetics factors, and certain surgical procedures. Patients characteristics associated with increased risk include female gender three times more frequently than males, history of PONV or motion sickness, and nonsmokers. Volatile agents are by far the most emetogenic factor known with 11 times the risk. Other anesthetic factors include intraoperative and postoperative use of opioids, nitrous oxide, neostigmine, and anesthetic lasting longer than 60 minutes have all been shown to increase risk. Laparoscopic procedures, gynecological, strabismus, plastic, ENT, and orthopedic procedures are most often associated with increased incidence of PONV. No screening model has shown greater than 70% accuracy in predicting PONV, but the simplified risk scores have shown the most promise because they are reliable and easy to use. Female gender, history of PONV or motion sickness, nonsmoker, intraoperative and postoperative opioids, and duration of surgery greater than 60 minutes are known to increase risk. Being able to quickly screen and identify patients at increased risk for PONV allows for individualization of prophylactic therapy to benefit those patients at greatest risk.

The safest and most cost effective means of prophylactic treatment of PONV is to provide the appropriate number of interventions that will reduce risk without increasing the risk of adverse effect to patients. Once risk is determined, strategies to decrease baseline risk should be employed. Regional anesthesia is known to be less emetogenic than general anesthesia and should be utilized when appropriate for patients with moderate to high risk for PONV. According to baseline risk, a planned approach to prophylactic treatment should be implemented. No single antiemetic approach has proven to be statistically more effective than any other antiemetics. Combination therapy with two agents from different classes is effective when baseline risk is moderate to high. Multimodal therapy has proven to be 98% effective and should be employed for patients at highest risk for developing PONV. A flow diagram will be a useful tool to guide the anesthetic provider in choices and appropriate treatment to maximize the reduction of risk of postoperative nausea and vomiting.

CHAPTER III

DEVELOPMENT OF A PONV ALGORITHM

In recent years much information has been published on the incidence and risk factor identification to determine best practice for management of postoperative nausea and/or vomiting. PONV has been an ongoing problem for several decades and though some advances have been made it remains a prevalent problem and has been identified by patients as a top priority to avoid following surgery. In this chapter I will discuss the population to which this algorithm is most applicable and identify characteristics which increase patient risk for development of PONV. I will also discuss the methodology for development of the algorithm; this was accomplished through review of consensus opinion from the literature and incorporating recommendations from consensus guidelines and published articles from experts in the field.

Population

Patient undergoing procedures with general anesthesia have a 30 percent chance of developing postoperative nausea and vomiting. All patients undergoing surgical procedures are at risk for developing PONV; however, certain characteristics of the patient, the anesthetic technique, and the surgical procedure have been implicated in increasing the risk. Koivuranta et al. (1997) and Apfel et al. (1999) developed simplified risk scores and determined the same characteristics were significantly correlated with increased risk of development of PONV. These characteristics are female gender, history of postoperative nausea or vomiting, history of motion sickness, nonsmoking status, and use of postoperative opiates. In a comparative study a six risk predictive models, Apfel, Kranke, Eberhart, Roos, and Roewer (2002) determined the use of the simplified risk scores, developed by Koivuranta et al. (1997) and Apfel et al. (1999), provided better discrimination and calibration properties than the other models and surpassed the other models on ease to use. Since these simplified risk scores have shown in a comparative study to have improved predictability and ease of use (Apfel et al., 2002), the screening of all patients for the primary risk factors should be completed on all patients undergoing surgical procedures and can be accomplished easily during the routine obtaining of the history and physical.

Methodology/Procedure

Algorithms or "decision tree" are streamlined and easy to use tools for rapid decision making. An algorithm is designed to start with initial data then branch in a logical fashion using yes or no responses to guide the practitioner through steps of assessment and management, branches that do not apply to the patients are disregarded; thereby streamlining decision making. After extensive review of the literature and summarization of several existing review articles on PONV, an algorithm was developed. As discusses above, the use of the simplified risk score that requires screening for only four factors shown to increase the risk of development of PONV has good discrimination and ease of use. As supported by Apfel et al. (2002) and Biedler et al. (2004), using a simplified risk stratified approach and adjusting treatment according to risk can reduce the incidence of PONV. These simplified risk scores are the primary risk factors screened for in the algorithm and each factor carries the same weighted value (see Figure

1). The number of risk factors each patient has is counted and used, along with duration of surgery, to determine if the patient is considered low, moderate, or high risk for the development of PONV. Apfel et al. (1999) determined that the presence of no risk factors was equivalent to a 10% risk, while 1, 2, 3, and 4 risk factors each conferred a risk of 21%, 39%, 61%, and 79% chance of PONV respectively.

Female Gender History of PONV or motion sickness Nonsmoker Intraoperative and postoperative opiates	Risk Equivalent by factors 0 = 10% 1 = 21% 2 = 39% 3 = 61% 4 = 79%

Figure 1. Risk factors for postoperative nausea and vomiting. The risk factors are shown on side 1 of the pocket guide. Each risk factor the patient has is counted; this corresponds to the risk equivalent and determines the patient's baseline risk.

Sinclair et al. (1999) determined the each thirty minute increase in duration of surgery increased the baseline risk by 59%. This finding is endorsed by Gan et al. (2003) and Habib and Gan (2004) to support recommending a 60% increase in risk for every thirty minute increase in duration of surgery. An example of how this can be applied is a patient has no risk factors from the simplified risk scores which is equivalent to a 10% baseline risk and surgery is of 30 minutes duration which would increase the risk to 16%.

Baseline risk is determined by the presence of these risk factors; female gender, nonsmoking status, history of PONV or motion sickness, and intraoperative and postoperative opiate use, and anticipated duration of surgery. These elements are then used to classify patients as low, moderate, or high risk for the development of PONV. After classification of baseline risk, treatment options flow through the use of an algorithm. The algorithm is a series of steps that requires the clinician to assess the situation and make treatment decisions based upon the selected responses. Treatment options are further subdivided according to risk class (see Figure 2).

Low risk is considered to be approximately 30%, moderate risk is 30-60%, and high risk is greater than 60%. Once the risk category is determined, this guides decision-making for appropriate interventions to minimize development of PONV. Patients falling into the low risk category do not require any interventions unless the medical sequela of vomiting can cause complications. An example of this would be vomiting following hiatal hernia or Nissen fundoplication. Vomiting that occurs following these surgeries could cause disruption of sutures or wound adhesion, resulting in bleeding which may necessitate a return to the operating room. No intervention is indicated for patients in the low risk class, as Watcha and Smith (1994) determined prophylactic therapy was only cost-effective when the risk of emesis exceeded 33%. Apfel and Roewer (2003) agreed that the prophylactic treatment of low risk patients was not indicated because even with a highly effective therapy, the number needed to treat was 10. With a 10-30% baseline risk in this group, the benefit did not exceed the cost-effectiveness or risk of adverse effects.

General anesthesia has a 10 fold increase in risk for development of PONV (Sinclair et al., 1999) compared to other anesthetic techniques; thereby avoiding general anesthesia when applicable is first line therapy for prophylaxis of PONV. For all patients with baseline risk in the moderate to high categories, regional anesthetic techniques should be considered and when appropriate be the primary anesthetic technique. If regional anesthetic techniques are not indicated, other interventions to minimize the risk of producing PONV should be considered and initiated when applicable. The use of

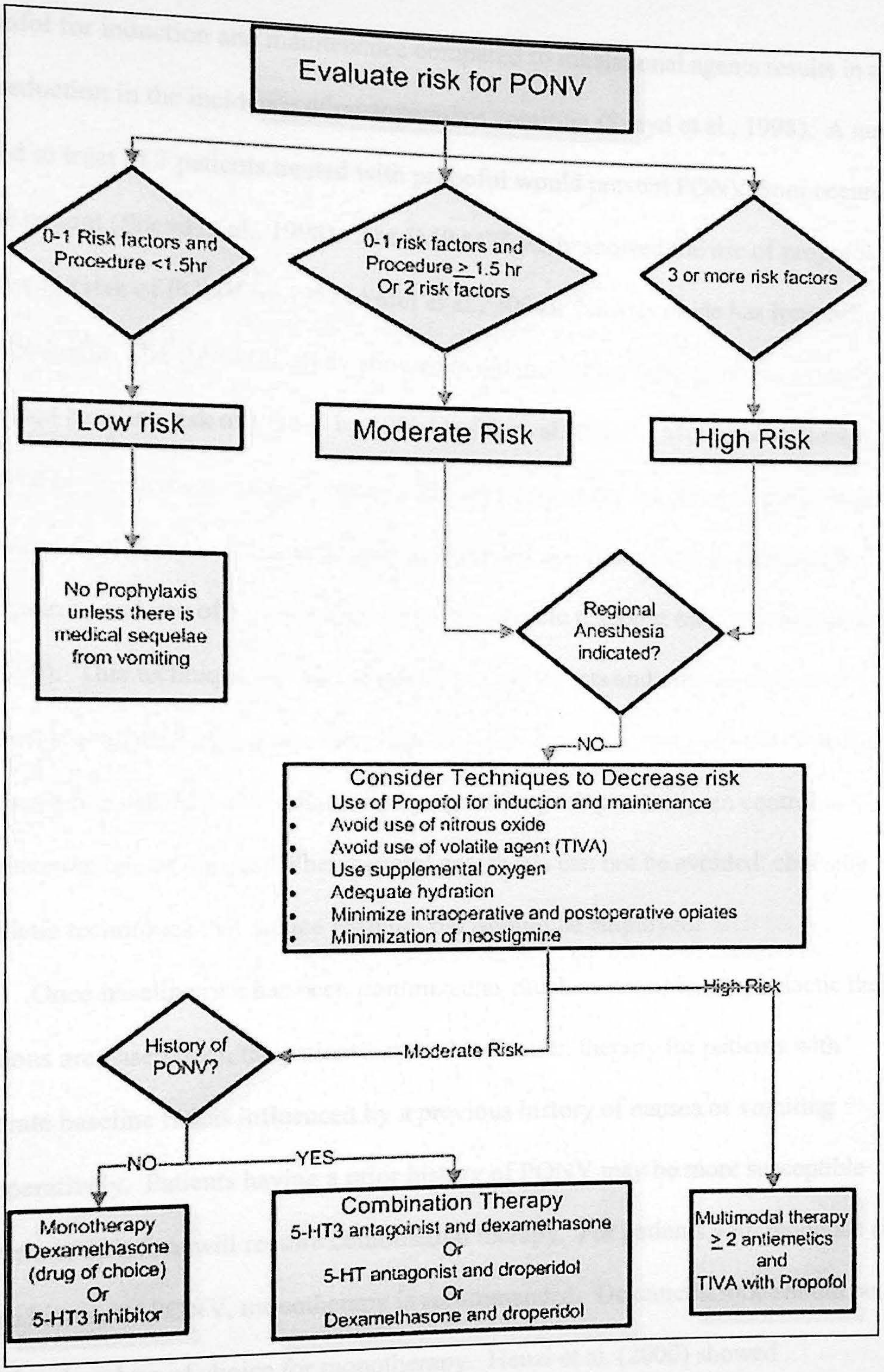

Figure2. PONV Algorithm. The algorithm is side 2 of the pocket guide.

propofol for induction and maintenance compared to inhalational agents results in a 3.7 fold reduction in the incidence of postoperative vomiting (Sneyd et al., 1998). A number needed to treat of 7 patients treated with propofol would prevent PONV from occurring in one patient (Sneyd et al., 1998). The IMPACT study showed the use of propofol reduces the risk of PONV by 19% (Apfel et al., 2004). Nitrous oxide has long believed to emetogenic. The IMPACT study showed avoidance of the use of nitrous oxide decreased baseline risk of PONV by 12% (Apfel et. al., 2004). Multimodal therapy using propofol by continuous infusion combined with remifentanil; aggressive intravenous hydration; combination antiemetic therapy with dexamethasone, droperidol, and ondansetron; and use of Ketorolac provides a complete response rate of 98% (Scuderi et. al., 2000). This technique avoids the use of volatile agents and nitrous oxide and neuromuscular blocking agents, thereby avoiding the need for reversal with neostigmine; and uses a nonsteroidal anti-inflammatory agent for postoperative pain control to minimize the use of opiates. When general anesthesia can not be avoided, choosing anesthetic techniques that reduce baseline risk should be employed.

Once baseline risk has been minimized as much as possible, prophylactic therapy decisions are based upon the patient's risk. Medication therapy for patients with moderate baseline risk is influenced by a previous history of nausea or vomiting postoperatively. Patients having a prior history of PONV may be more susceptible recurrence, therefore will require combination therapy. For patients with moderate risk and no history of PONV, monotherapy is recommended. Dexamethasone should be considered as drug of choice for monotherapy. Henzi et al. (2000) showed corticosteroids have superiority to placebo and are comparable to other antiemetics in short term prophylaxis with increased efficacy in long term prevention of PONV. Dexamethasone shows no adverse effects when given as a one-time dose for the prevention of PONV. Dexamethasone also has the added benefit of being a cost-effective alternative (Apfel & Roewer, 2003; Gan et al., 2003). Additional choices for monotherapy include a serotonin 5-HT receptor antagonist, droperidol, transdermal scopolamine, or other antiemetic.

In patients with moderate baseline risk and a previous history of PONV, initial therapy should consist of combination therapy with two agents from different classes. "Combination therapy is superior to monotherapy for PONV prophylaxis" (Gan et al., 2003, p. 67), therefore it is recommended for use as the baseline risk increases. The addition of each anti-emetic agent decreases the risk by 26% (Apfel & Roewer, 2003). The 5-HT3 receptor antagonists have been shown to have better anti-vomiting properties than anti-nausea properties. In this class, the effects of anti-vomiting would be the most desirable effect and a 5-HT3 antagonist should be considered the drug of choice in combination with another agent. The 5-HT3 antagonist should be paired with dexamethasone or droperidol as these drugs have proven anti-nausea effects (Gan et al., 2003).

In patients with highest risk, having 3 or 4 risk factors, the rate of PONV is as high as 60%. These patients require special consideration when planning interventions to prevent PONV. Regional anesthesia and interventions to minimize risk should be employed to the extent allowable. A multimodal approach to prophylactic management is desirable. The use of a multimodal approach which includes the use of TIVA with propofol; avoiding volatile agents and nitrous oxide, combination therapy with 3 agents, and use of none drug related intervention has resulted in a complete treatment in 98% of patients (Scuderi et al., 2000). Combination therapy should always include drugs from a different class.

Evaluation

The pocket guide was evaluated by a group of anesthetic providers which included a first year student nurse anesthetist, a second year student nurse anesthetist, a CRNA with less than two years experience, and a CRNA with approximately eight years of experience. This group was chosen because it encompassed the providers for whom the pocket guide was intended and an experienced CRNA who would be considered in the expert stage per Benner's model. The providers evaluated the pocket guide on overall quality which included applicability, readability, and functionality. The panel also evaluated each component separately for clarity and purpose.

All members of the evaluation panel felt the pocket guide was applicable to practice and the providers in the novice and advanced beginner stages felt this guide would augment practice. The panel agreed the PONV Algorithm pocket guide was clearly written and easy to follow. The algorithm clearly delineated treatment options based upon baseline risk and strategies to minimize risk. Screening criteria were clear; however, it was recommended to separate the simple screening criteria from the other factors associated with increased and provide a simple instruction. This addition was made to page one of the PONV Algorithm pocket guide (see Figure 3). Overall, the panel determined the PONV Algorithm pocket guide was precise, to the point, and easy to understand. The panel described the pocket guide as a guick reference and great resource for the novice and advanced beginners.

Risk Factors

Simplified Risk Score

Female Gender
History of PONV or motion sickness
Nonsmoker
Intraoperative and postoperative opiates

Anticipated risk by factor
0= 10%
1=21%
2=39%
3=61%
4=79%

Evaluate all patients for presence of above risk factors. Count number of factors present to determine baseline risk.

Other Factor Associated with Increase Risk

Anesthetic factors that increase risk

- Intraoperative use of volatile agents
- Use of nitrous oxide
- Use of intraoperative and postoperative opioids

Surgical factors that increase risk

- Duration of surgery (each 30 minute increase in duration increases baseline PONV by 60%)
- Type of surgery
  - o Laparoscopy
  - o Ear-nose-throat surgery
  - o Neurosurgery
  - o Breast surgery
  - o Strabismus surgery
  - o Laparotomy
  - o Plastic surgery

Figure 3. PONV Risk Factors. This is page one of the PONV Algorithm Pocket guide includes simplied risk score screening, simple instructions of use, and other factors known to increase risk.

Conclusion

PONV has long been a problem following surgery, consider the ether era when PONV was so common it was thought to be a natural consequence of general anesthesia. Initial research focused on ways to manage nausea and vomiting once it developed. Research focus in the last several decades is identification of risk factors and the prevention of the development of PONV. Progress has been made; however, current best practice in the management of PONV finds an incidence still around 20-30%. Several drugs exist that have antiemetic properties yet side effects and costs vary greatly, therefore nondiscriminatory use of these agents can placed patients at risk of unwarranted side effects and increase health care costs.

A consensus guideline of multidisciplinary experts published by Gan et al. (2003) recommended a treatment approach to manage PONV. While this systematic guideline provided a framework of PONV treatment, there is variation in treatment recommendations among experts in the field on the management of PONV. Apfel and Roewer (2003) and Habib and Gan (2004) also created a systematic treatment approach to the prevention of PONV. Each of these guidelines contains similar main principles but vary slightly in screening criteria and treatment options. This project's algorithm has combined the major principles outlined in each guideline recommendation and incorporates differences when supported by literature to formulate one algorithm.

A panel of anesthesia providers comprised of students in nurse anesthesia program and practicing CRNA's. The panel evaluated the PONV Algorithm pocket guide for applicability, readability, and ability to guide decision-making. The panel felt the project to be resourceful for novice and advanced beginners stages of Benner's model. The panel agreed the pocket was easy to follow and clearly written making treatment decisions simple. The panel recommended adding to the screening criteria a simple instruction guide and inclusion of other factors known to increase risk of PONV development. These changes were incorporated and are shown in Figure 3. After changes were made the panel agreed the changes improved the applicability and easy of use.

Use of algorithm is a very useful tool for novice, advanced beginners, and competent nurses as described in Benner's theoretical model of nursing practice. Nurse's in the novice and advanced beginner stages are mostly guided by rules and function in a context free environment. The algorithm provides a set of guidelines or rules for which situations need to be contemplated with a definitive plan of action. The nurse anesthesia students, considered novice and advanced beginners, who evaluated the guide particularly felt this PONV Algorithm pocket guide is very applicable to practice and would greatly enhance decision-making for treatment options. According to Benner's model, competent nurses identify consistency, predictability, and time management as priorities for planning care. Use of PONV Algorithm pocket guide provides a consistent and predictable means to manage PONV for patients. This reliable and expected method allows the competent to begin to evaluate the outcomes of standard care and recognize patterns thereby enhancing clinical learning.

Using algorithms is an easy way to guide healthcare providers in the decision-making process. An algorithm should be created utilizing existing scientific evidence and incorporating expert consensus. This project's algorithm has been made into a pocket guide, which includes screening criteria on side one and the algorithm on side two. This pocket guide will be beneficial to the novice, advanced beginner, and competent nurse in decision-making process until they develop that intuitive feeling, way of knowing, and develop into a proficient practitioner.

CHAPTER IV

DISCUSSION

Implications for Nursing

The PONV Algorithm pocket guide is designed to be a useful tool to assist the nurse anesthetist in decision-making for management of patients. This tool is designed not only to benefit patients by providing a streamlined approach to the management of postoperative nausea and vomiting but can also benefit the nursing profession. In this chapter, this project's affect on the practice, research, education, and policy of the nurse anesthesia profession will be discussed.

Practice

The PONV Algorithm pocket guide is designed to serve as a clinical tool in the decision-making process and provide guidance for nurse anesthetists just beginning to practice in their expanded role. The pocket guide provides the less experienced nurse anesthetist with clear, specific guidelines for practice and eliminates the ambiguity of many different treatment options. The use of the PONV Algorithm pocket guide will reduce variability in practice and promote continuity of care, which can be useful to even experienced nurse anesthetists. However, many clinicians describe this sort of tool as practicing "cookbook" medicine and feel it prevents individualization of care which is specific to each patient. This pocket guide however, is designed to account for several variations in patient characteristics. Another benefit of the pocket guide is it provides a standardized tool for which data can be collected to evaluate practice and patient outcomes.

Research

Nausea and vomiting remain persistent problems following general anesthesia and no single approach has proven to be 100% effective in the prevention of PONV. Although much progress has been made, the incidence of PONV remains at 20-30%. A systematic approach to prevention of PONV based upon risk has merit and provides as cost-effective approach while minimizing potential side effects by not over treating patients. The PONV Algorithm pocket guide could further research in this area by first testing ease of use among students in nurse anesthesia programs and newly graduated nurse anesthetists. The algorithm could also be used to study effectiveness in the reduction of PONV by providing a standard screening mechanism and the determining treatment options bases upon the patients underlying risk. Research could also be conducted to evaluate the cost-effectiveness of the varying treatment options to determine best practice. Research in the area of PONV is lacking in clearly defined treatment end-points, as studies evaluate the time differently as to short term and long term effects, thereby making to difficult to compare various therapeutic options. Some research currently in also being conducted to evaluate nonpharmacological intervention for the prevention and treatment of PONV. As nonpharmacological interventions develop, they should be considered for inclusion in the algorithm. Patient and nursing satisfaction should also be considered as treatment end-points for evaluation on effectiveness of the treatment options as outlined in this algorithm. Creation of the algorithm based upon existing knowledge can be considered the beginning to further research as anesthesia continues to find way to prevent patient suffering from postoperative nausea and vomiting.

Education

The use of the pocket guide can easily be incorporated in nurse anesthesia programs and used readily during the training process. Novice nurse anesthetists, people in training programs, require rules and guidelines as a foundation for practice and often have difficulty determining relevant from irrelevant aspects the use of clearly defined pocket guide can be instrumental. The pocket guide clearly defines which areas to screen for and then based upon the presence of risk factors the treatment options are outlined, enabling educators to use this tool during teaching sessions.

Policy

Algorithms and pocket guides should reflect the minimum standards of care and thus should be broad enough to be implemented with all patients. While these tools are designed to meet best practice standards, one must be careful not make them to strict so that any deviation from care can expose the practitioner to litigation. At a minimum, this PONV Algorithm pocket guide is designed to be compliant with the American Association of Nurse Anesthetists (AANA) standards I, III, and IV (AANA, 2005). These standards require completion of a comprehensive preoperative evaluation, formulate a patient specific plan of care, and assess and adjust the plan of care based upon the patient's physiological response.

After thorough evaluation of patient outcomes this algorithm could easily be implemented into departmental policies and procedures on the management of PONV. More work needs to be done, however, to test its validity and reliability on patient outcomes and expanded to include the management of existing PONV once the patient has failed prophylactic treatment.

Summary

This pocket guide is easy to use for the beginner to nurse anesthesia as an augmentation to practice. Algorithms provide a series of "rules" to guide the novice, advanced beginner, and competent nurse in practice as primarily there development is focusing on rules for decisions in practice. Creation of tools, such as the pocket guide provides standardized treatment options and is a good foundation from which research can flow to advance the profession of nurse anesthesia. Education can be enhanced with the assistance of guides that summarize and streamline complex medical issues. These devices breaks the situation down into a series of manageable parts and enhance learning. Algorithms must be developed utilizing consensus of experts in the field when applicable and must reflect evidenced based practice. The PONV Algorithm pocket guide incorporates the latest published consensus reports and recommendations from experts in the area of postoperative nausea and vomiting. The Algorithm maintains minimum AANA standards. After evaluation of patient outcomes, the algorithm could easily be incorporated into policies in healthcare institutions for prophylaxis of PONV. PONV remains a pervasive issue for anesthesia providers and is a high priority to be avoided by patients following surgery. Prevention of the occurrence of nausea and vomiting can improve satisfaction for both patients and healthcare providers.

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