INTEGRATIVE TREATMENT OF POSTOPERATIVE NAUSEA AND VOMITING:

A BEST PRACTICE APPROACH

By

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Table of Contents

Abstract 4

CHAPTER 1 5

Introduction 5

Statement of Purpose 5

Background of Issue Importance 5

Significance of Problem 6

Summary 8

CHAPTER 2 10

Review of Literature 10

Aromatherapy: Ginger Essence, Peppermint Oil and Isopropyl Alcohol 10

Acupuncture of Pericardium 6 Acupressure Point 27

Supplemental Inspired Oxygen 37

Supplemental Intravenous Fluid Therapy 46

Serotonin $5HT_3$ Antagonists 56

Conclusion 66

CHAPTER 3 68

Best Practice Recommendations: Prevention and Treatment of PONV 68

Table 1 70

Table 2 72

Table 3 74

Table 4 75

Table 5 77

CHAPTER 4 79

Implementation to Nursing Practice and Evaluation 79

Implementation 80

Table 6 81

Evaluation 84

Strengths and Limitations of Honors Thesis 85

Summary 88

References 90

Abstract

The purpose of this thesis was to create best practice recommendations to treat postoperative nausea and vomiting (PONV) during the first 24 postoperative hours in patients undergoing general anesthesia. PONV is a multifaceted and unpleasant phenomenon, increasing length and cost of stay. Pharmacotherapy is most often used to treat PONV though it may not be the most cost-effective intervention nor patient preference . The literature review was conducted through CINAHL, Embase and PubMed. The keywords used to search were PONV, postoperative nausea and vomiting, aromatherapy, P6 acupuncture, supplemental oxygen, supplemental fluid therapy, intravenous fluid therapy, pharmacotherapy, ondansetron, and $5HT_3$ antagonists. Dates of publication were limited to 2008 to 2018. The literature revealed evidence to support using acupuncture on the P6 acupoint site (N = 5), supplemental intravenous fluids with crystalloids (N = 4) and the use of ondansetron as a first line antiemetic in combination with dexamethasone (N = 4). Based on these results, a best practice recommendation for integrative nursing to treat PONV includes a bundle of interventions of controlled breathing, acupuncture of the P6 acupoint, intraoperative supplemental intravenous fluid of 30 mL/kg/hour crystalloid solutions, and the use of ondansetron as a first line antiemetic therapy combined with dexamethasone.

CHAPTER 1

Introduction

Statement of Purpose

The purpose of this thesis is to create best practice recommendations to better treat and prevent postoperative nausea and vomiting (PONV) during the first 24 postoperative hours in patients recovering from procedures under general anesthesia. The best practice recommendations will be developed using evidence based research and the principles of integrative nursing focusing on a range of interventions from least to most invasive for PONV (Cutshall & Van Getson, 2014). The background information on the importance of this issue will be discussed as well as the relevance of this issue as related to the field of nursing practice. After reviewing and critically analyzing the background information, the relevance to nursing, and findings from evidence based research, a best practice recommendation will be proposed and detailed with the objective of finding methods of treating PONV for patients in the first 24 hours after recovering from general anesthesia with an integrative approach.

Background of Issue Importance

Several medications used for anesthesiology and following surgical procedures can cause nausea and vomiting. These symptoms are not only unpleasant for the patient and affect their quality of life, but can also lead to a host of negative consequences. There is an important distinction between nausea and vomiting in which nausea is an unpleasant and subjective feeling of the need or urge to vomit often associated with tachycardia, flushing and pallor, while vomiting is the point at which the abdominal muscles contract forcefully and result in the "expulsion of stomach contents" (Cuthshall & Van Getson, 2014, p. 215). Singh, Yoon and Kuo (2016) name nausea as the "neglected symptom" (p. 98) due to the fact that many of the current

therapies used aim to alleviate vomiting or to improve the motility of the gastrointestinal tract. Additionally, acute nausea is considered to be nausea that occurs within 24 hours of a trigger or after taking a medication and delayed nausea is considered to be any nausea that develops 24 hours after a trigger or after taking a medication (Cutshall & Van Getson, 2014).

Evidence has shown that PONV can increase the medical costs related to increased time spent in the PACU (post-anesthesia care unit), increase recovery times, affect patient satisfaction with care, and can even cause significant postoperative complications (Cutshall & Van Getson, 2014). As many as 20% to 30% of all surgical patients will experience PONV though the prevalence of PONV for those with a number of risk factors can reach as high as 70% to 80% (Cutshall & Van Getson, 2014). Current pharmacotherapies used to treat PONV are additive in that they decrease the relative risk of PONV by about 25% each time greatly improving PONV, however this also means that the current pharmacological approaches fail to fully eradicate PONV (Horn, Wallisch, Homanics & Williams, 2014).

Significance of Problem

PONV is thought to be caused by a number of interacting factors and is commonly attributed to the inhaled anesthetics used during surgery, opioids used to manage pain postoperatively, pain that has gone unrelieved, hypotension and early oral intake (Cutshall & Van Getson, 2014). Additionally, specific types of procedures and preexisting medical conditions may also increase the risk of PONV (Cutshall & Van Getson, 2014). Procedures that are thought to predispose patients to develop PONV include laparoscopic procedures, gynecological procedures, cholecystectomies, and surgeries involving the ear, nose or throat (Horn et al., 2014). Horn et al. (2014) site the biggest risk predictors of developing PONV to be

being of a young age, being a non-smoker, being a female, and having a personal or family history of motion sickness.

Horn et al. (2014) admit there are many pathophysiological pathways involved in nausea and vomiting and, due to the fact that nausea cannot be "directly measured in non-human animals" (p. 58) the neurobiology of nausea is not fully understood. The caudal hindbrain houses the neural circuits involved in emesis including the respiratory nuclear groups found in the reticular formation and the nucleus of the solitary tract (Horn et al., 2014). According to Horn et al. (2014) activation of "descending pathways from the forebrain" (p. 58) can also produce vomiting. Evidence shows that inhaled anesthetics can produce emesis by affecting the vestibular system, "stimulate vagal afferent fibers" (p. 58), and enhance the function of 5-HT_3 receptors (Horn et al., 2014). Because surgical procedures often cause inflammation, it is possible that some of PONV is due to inflammation and the antiemetics used to control PONV such as 5-HT_3 antagonists are effective due to the anti-inflammatory properties (Horn et al., 2014). Lastly, evidence has shown that the vomiting center can be activated by the stimulation of the gastrointestinal tract by nitrous oxide used during surgical procedures (Cutshall & Van Getson, 2014). While there are many potential causes of PONV, it is clear that both the opioids used to manage postoperative pain and the inhaled anesthetics used during surgery disrupt the gastrointestinal tract and cause "gastrointestinal dysrhythmias" (p. 59) which are known biomarkers for both vomiting and nausea (Horn et al., 2014).

Parra-Sanchez et al. (2012) conducted a study to analyze the cost of PONV in 100 patients undergoing ambulatory surgeries. The study looked at the time the staff spent with each patient, the incidence of PONV, the duration of recovery, the supplies used to treat PONV, and quality of life of patients experiencing PONV up to the third postoperative day (Parra-Sanchez et

al., 2012). Parra-Sanchez et al. (2012) found that when compared with patients who did not experience PONV, those who experienced PONV spent one hour longer in the PACU (p = 0.001), had a significantly higher time spent with the nursing staff (p = 0.02), had significantly higher costs for postoperative recovery, a difference between $730 and $640 ($p$ = 0.006) and had reported significantly worsened qualities of life (p < 0.001). It was found that patients would be willing to pay an additional $75 dollars to avoid PONV and the decreased quality of life associated with PONV (Parra-Sanchez et al., 2012).

As stated by Cutshall and Van Getson (2014), a nurse using an integrative approach looking at nausea looks at the whole person as a system and looks for all potential causes and interventions for PONV. The integrative nurse should then move from the least invasive intervention possible to more invasive with the goal of facilitating the natural process of healing (Cutshall & Van Getson, 2014). When considering this integrative nursing approach, it is clear that not one intervention will be completely effective for all patients and that not all patients require the same invasiveness of intervention.

Summary

The purpose of this thesis is to develop a best practice recommendation to better treat PONV in the first 24 postoperative hours both in the PACU and following discharge in patients undergoing procedures with general anesthesiology using a variety of interventions with an integrative approach. Parra-Sanchez et al. (2012) showed that PONV can not only worsen quality of life but increase time spent in the PACU, increase the time demands on nursing staff, and increase patient costs. Though there are many promising and helpful pharmacological treatments for PONV, none of them fully eliminate PONV (Horn et al., 2014). This thesis is intended to discover not only which treatments are beneficial for treating PONV, but also to determine

which treatments and interventions need more research and can be improved upon. With the information gathered throughout this thesis, evidence based best practice recommendations can be developed to better treat acute PONV in patients who went under general anesthesiology.

CHAPTER 2

Review of Literature

To complete the literature review included in this thesis, searches of PubMed, CINAHL and EmBase were conducted for articles published between the years of 2013 and 2018 in peer reviewed journals. Search parameters were expanded to include articles published as early as 2008 if results from initial searches did not yield a sufficient number of articles or articles of good quality and rigorous study design. Search keywords included "postoperative nausea and vomiting OR PONV" with subheadings of "aromatherapy," "P6 acupuncture," "acupuncture," "supplemental oxygen," "oxygen," "supplemental fluid therapy," "intravenous fluid therapy," "pharmacotherapy," "ondansetron," and "$5HT_3$ antagonists." A total of 27 articles were selected to be included in the literature based on time of publication, study design, and the type of intervention examined for prevention and treatment of postoperative nausea and vomiting (PONV). The information provided in these 27 articles will be synthesized to create a best practice recommendation for the prevention and treatment of PONV with an integrative approach.

Aromatherapy: Ginger Essence, Peppermint Oil and Isopropyl Alcohol

Investigating the Effects of Inhaling Ginger Essence on Post-Nephrectomy Nausea and Vomiting

Adib-Hajibaghery and Hosseini (2015) assert that there is little known information about the relationship between inhaled ginger and PONV, however it is known that the active ingredients in ginger have anti-inflammatory, antiemetic and antipyretic properties and also reduces gastrointestinal distress. The purpose of their randomized control trial with level of evidence of II, was to determine and evaluate the effectiveness of inhaled ginger essence on

PONV in post-nephrectomy patients under general anesthesia. Convenience sampling was used to recruit 120 patients from a teaching hospital in Iran. Inclusion criteria consisted of being of American Society of Anesthesiology (ASA) class II status, being a participant 18 years of age or older, being able to speak and write Persian, having no known allergies to ginger, having no balance hearing or impairments, having no known history of allergies, motion sickness, asthma or olfactory problems and having nothing by mouth for at least eight hours, no antiemetic medications for at least 24 hours and no chemotherapy for 18 to 48 hours before surgery. Exclusion criteria for the study included developing any reactions or sensitivities to ginger, withdrawal from the study, and developing acute hemodynamic instability. In order to prevent crossover between the intervention of inhaling ginger essence and control of inhalation of normal saline, the participants on the first day were randomly assigned to the intervention with a coin toss, and following the first day alternations between control and intervention took place until completion of study. A power analysis was conducted and determined that each group would need 51 participants to yield statistically significant results. In the end, each group had a total of 60 participants to allow for possible drop out however there was no attrition. A two inch by two inch gauze pad with either two drops of normal saline, or two drops of ginger essence was attached to patients' clothing every 30 minutes for two hours in the recovery unity and once again at the sixth hour on the ward. Data was conducted with a visual analog scale (VAS) on a scale of one to ten with zero being "no nausea" and ten being "most severe nausea" every hour for the first six hours following surgery (Adib-Hajibaghery & Hosseini, 2015). Each group was compared with Chi-squared tests and Fisher's tests. Variance analysis was completed both between and within groups with statistical significance set at $p \leq 0.05$. Demographics between groups were not statistically significant save that of amount of blood transfused ($p = 0.02$) which

was higher in the experimental group than control group, and systolic blood pressures ($p = 0.01$) and mg of ondansetron administered ($p = 0.02$) which were both lower in the experiment group than control group. Results from the study indicate that the number of episodes of vomiting were significantly lower at T4 and were significantly lower for the intervention group ($p < 0.001$). Additionally, the mean nausea intensity scores were consistently higher in the control group until the sixth hour following surgery ($P < 0.001$) and the mean nausea score did not decrease significantly for the control group. On the other hand, the mean nausea scores did decrease for the intervention group ($p < 0.001$). The rescue antiemetic of ondansetron was administered to patients who had severe or moderate nausea after they met with a physician. The dose of ondansetron administered was significantly higher in the control group than the intervention group ($p = 0.001$). The authors conclude that inhaled ginger essence is beneficial for management of PONV and can be used as an effective antiemetic, however, further studies need to be conducted with inhaled ginger essence in larger populations. The authors note that their findings are not consistent with several studies that indicate that ginger either has no effect on PONV or increased the incidence of nausea. Additionally, the authors note that the results could have been altered by shallow breathing of patients in recovery caused by the general anesthetic. The authors hypothesize shallow breathing may have limited the absorption of the ginger essence, however shallow breathing was observed in both control and intervention groups and therefore would have affected each group equally. Because of the contradictory results of this study in relation to other studies, as well as the very specific sample for this study, the results should be interpreted with caution and may not be generalizable or applicable to larger clinical populations.

Effectiveness of Ginger Essential Oil on Postoperative Nausea and Vomiting in Abdominal Surgery Patients

Lee and Shin (2017) conducted a quasi-experimental study with level of evidence of III in Seoul, South Korea to determine the effectiveness of ginger essential oil aromatherapy on PONV in patients who underwent major abdominal surgeries. Convenience sampling was used to recruit a total of 60 patients from three different surgical units in the same hospital in Seoul. Inclusion criteria included being scheduled for major abdominal surgeries including gallbladder, liver, appendix and pancreas surgeries, being between 20 and 70 years of age, being under general anesthesia for at least 60 minutes, ability to understand the study, being alert and oriented to time, place, situation and person upon admission and requesting patient controlled analgesia (PCA) postoperatively for pain. Exclusion criteria included having severe kidney, heart or lung diseases, having allergies to medications or ginger essence or other essential oils and those receiving chemotherapy. The authors conducted a power analysis and determined a target sample size of 30 participants in each group to yield results of statistical significance. Thirty participants were assigned to each group with no attrition yielding a total of 60 participants with 30 in each group. Participants were not randomly assigned and instead the first 30 participants meeting inclusion and exclusion criteria received the intervention of inhaled ginger essential oil and the following 30 received the control intervention of inhaled normal saline. The non-random assignment of groups was done in order to ensure that in the recovery area there would not be additional inhalants that would alter the results of the study. Upon arrival in the recovery unit after leaving the post-anesthesia care unit (PACU), patients were given an aromatherapy necklace which contained 0.3 mL of normal saline or 0.3 mL of organic ginger essential oil to wear for the first 24 postoperative hours. A version of the Index of Nausea, Vomiting and

Retching (INVR) scale was used to collect data on a numerical scale from zero to 32 with 32 being severe nausea. Participants were asked about both the duration and intensity of their nausea, vomiting and retching at six, 12 and 24 hours after initiation of aromatherapy. Comparisons between groups were analyzed with *t* tests and Chi-squared tests, interrater reliability was assessed with a Cronbach's alpha coefficient of 0.94 and statistical significance was deemed to be $p \leq 0.05$. The authors found that the mean scores of PONV were significantly lower for the intervention group than the control group ($p < 0.001$). Additionally, the interaction between group and time was statistically significant ($p < 0.001$) meaning that the changes in mean PONV scores between the groups was significantly different over time with the intervention group experiencing a faster decline in PONV scores. Finally, mean PONV scores were significantly lower for the intervention group than control group at six hours, 12 hours and 24 hours postoperatively ($p < 0.05$). While the authors conclude that inhaled ginger essential oil as aromatherapy is effective at reducing PONV in patients undergoing major abdominal surgery and is promising for PONV in general, they make sure to note that it is unknown at what time the beneficial effects of the intervention took place within the first six hours. The authors also include that it is impossible to blind both participants and researchers because the nature of the intervention is scent. The authors also assert that larger samples sizes in future research are needed and that this article did not evaluate the effectiveness of ginger essential oil aromatherapy while in the PACU. For the aforementioned reasons, the results of this study should be interpreted with caution.

Inhaled Peppermint Oil for Postop Nausea in Patients Undergoing Cardiac Surgery

Briggs, Hawrylack and Mooney (2016) assert that not only is PONV an unpleasant event for many patients but that it has special importance for cardiac patients' as the antiemetic of

choice for cardiovascular critical care complex (CVCCC), ondansetron, has a tendency to make patients drowsy and interfere with their compliance in ambulation and deep breathing exercises and has been reported to cause dysrhythmias. The authors of this study conducted a quasi-experimental study with no control and the intervention of a peppermint oil nasal inhaler with level of evidence of III. The purpose of this study was to determine how effective peppermint oil is in managing PONV in cardiac patients and to determine the level of patient satisfaction of management of PONV with peppermint oil. A power analysis was conducted and determined need of 30 participants to yield results of statistical significance of $p \leq 0.05$. In the end, 123 patients were enrolled through convenience sampling that was conducted in a large tertiary care and academic facility in Delaware on the step-down unit. Thirty-four participants were included in the study group after developing PONV and of those 34, only 30 completed the exit questionnaire. Included in those enrolled, were adult cardiac surgery patients who underwent implantable electronic lead revision, coronary artery bypass (CAD), thoracic aortic aneurysm repair, valve surgery, transcatheter aortic valve replacement and left-ventricular assist device implantation surgeries. Inclusion criteria for the study consisted of being at least 18 years old, being willing to try aromatherapy and being able to speak and understand English. Exclusion criteria for this study included having allergies to alcohol based products or peppermint and not being able to provide informed consent. One nurse prepared all inhalers independently which consisted of three drops of peppermint essential oil on a cotton wick. Each inhaler had a cap on both ends, four holes at the base of the inhaler and one opening at the other end used for inhalation through one naris. Upon the patient's first presentation of nausea, they were asked to self-report their level of nausea on a scale of zero to five with zero being "no nausea" and five being "nausea with dry heaves reported" (Briggs et al., 2016). The nurse then provided teaching

on the use of the inhaler which included holding inhaler up to the patient's naris of choice, closure of the other naris with fingers, inhalation for three seconds, holding of the breath for three seconds and exhalation through pursed lips for three seconds repeated a total of three times. Following the intervention, the nurse would then ask the patient to again report their nausea on the zero to five scale two minutes after the first report of nausea (Briggs et al., 2016). Following the protocol, participants were asked to report their level of satisfaction of the management of PONV from "not satisfied" to "very satisfied" on a scale of zero to ten, their willingness to try the protocol again in the future, and if they thought that peppermint oil should be used to treat PONV. Data was analyzed with Statistical Package for the Social Sciences (SPSS) software. Comparative *t* tests were used to compare pre-intervention and post-intervention scores. The authors found that the difference in mean nausea scores before and after using peppermint inhalers was significant ($p = 0.05$) with the post-use scores being lower. Additionally, 93% of participants who answered the exit survey reported being satisfied with management of PONV in this study and would be willing to try it again, and 90% of the participants who answered the exit survey reported that they thought peppermint oil should be one of the options presented for management of PONV. The authors state that their findings are consistent with other studies regarding the use of postoperative nausea (PON) and that peppermint oil and that peppermint oil aromatherapy is a cost-effective way to manage PONV and should be used routinely. The authors also note that further research is needed to identify the effect of peppermint oil on patients with gastrointestinal disorders. This study had several limitations including the use of multiple nurses in data collection and only using patients in the step-down unit as opposed to including patients in the intensive care unit (ICU). Additionally, this study would benefit from use of more study participants because a large portion of those originally enrolled did not present

PONV and therefore did not receive the intervention. The nurse teaching the intervention to the patient did not assess the patency of the nares before allowing the patient to choose which naris to inhale from which may have affected the absorption of the peppermint. Finally, there was no control or randomization in this study which greatly decrease the level of evidence. Because the results of this study were not comparative, it may have limited the generalizability of the results of the study.

Controlled Breathing With or Without Peppermint Aromatherapy for Postoperative Nausea and/or Vomiting Symptom Relief: A Randomized Controlled Trial

Sites et al. (2014) noted that much of what is known about aromatherapy for medical purposes is anecdotal but is also one of the three interventions contained in the ASPAN guideline for PONV management. For these reasons, the authors conducted a randomized control trial with a level of evidence of II to determine the efficacy of controlled breathing (CB) in conjunction with peppermint aromatherapy compared to a control group of CB alone on the effects of the symptoms of PONV. The setting for this study was a rural, non-profit hospital in North Carolina, USA, in the PACU, operative suite and surgery units. The authors conducted a power analysis and determined the need for 130 total subjects to be enrolled to achieve results of statistical significance of $p \leq 0.05$. Convenience sampling was used and a total of 330 subjects were selected with participants randomized by a computer generated program yielding 161 participants in control CB group, and 169 patients in the aromatherapy group. Because there were high levels of certified registered nurse anesthetist (CRNA) unavailability, high levels of attrition, and not all participants experienced PONV, only 16 participants in the CB control group and 26 participants in the CB with aromatherapy group produced data that could be analyzed. Inclusion criteria consisted of the ability to breathe through the nose, being 18 years or

older, being able to verbalize incidences of nausea and vomiting and participants were scheduled to receive ENT, orthopedic, urologic or laparoscopic surgeries under general anesthesia. Exclusion criteria included being nauseous or vomiting within 24 hours of surgery, having a history of menthol or peppermint allergies, having a history of alcoholism, being pregnant, being a patient from the department of corrections, having emergent surgeries over the weekend preceding the study or taking metronidazole or disulfiram. Participants were asked to describe the current nausea and vomiting on a zero to 10 descriptive ordinal scale (DOS) before surgery with zero being "none" and 10 being "the worst symptoms a subject could imagine" (Sites et al., 2014). Subjects each received a 13-dram vial with a cotton braid to hold under their nose during deep breathing with the control group not having anything on the cotton braid and the aromatherapy group having 500 mL of peppermint spirits applied to the cotton braid. Participants were instructed to deeply inhale through the nose for three seconds, hold their breath for three seconds, and exhale for three seconds repeating this for a total of three breaths after the initial presentation of PONV. PONV was assessed five minutes after the initial episode on the DOS and if symptoms remained, the intervention and assessment were completed once more. If the symptoms still remained after repetition of intervention, the patient was offered a rescue antiemetic. Data was collected on DOS scores, types of medications both intraoperatively and postoperatively, time on NPO, risk factors and demographics. Data was analyzed with standard deviations, frequencies and means as well as Chi-squared tests for categorical data. There were not statistically significant differences between groups in demographic data including gender and age. Out of the risk factors analyzed, being of female gender was the only statistically significant predictor of developing PONV ($p = 0.0024$). The authors found that as the number of risk factors for PONV increased from two to three to four, the incidence of PONV increased from 14%, 32%

to 83% respectively. The need for antiemetic therapy was similar between groups ($p = 0.76$) as was the effectiveness of intervention ($p = 0.61$). The authors conclude that peppermint aromatherapy used with CB is effective at controlling PONV symptoms, however it may not be more effective than CB alone. While these findings are clinically relevant, in order to comment with certainty there is need for future research. In the meantime, CB should be used perioperatively to reduce PONV symptoms as it can be initiated at the bedside at minimal cost to the facility. As mentioned previously, the study suffered from high attrition rates and CRNA unavailability requiring exclusion of several eligible participants. For these reasons the study did not yield statistically significant results and caused validity to decrease. Additionally, the authors state that this study solely evaluated the effectiveness on a single episode of PONV and not throughout the entire post-operative period. For various reasons, the results may not be of high quality and therefore may not be generalizable to larger populations or be clinically applicable.

Effects of Controlled Breathing, With or Without Aromatherapy, in the Treatment of Postoperative Nausea

Cronin et al. (2015) recognized that though there was some research indicating the positive effects of aromatherapy on PONV, few studies have been completed regarding isopropyl alcohol (IPA). Because of this lack of research, the authors conducted a study to compare the effectiveness of CB with and without inhaled IPA for management of postoperative nausea (PON) in adult female patients undergoing outpatient laparoscopy procedures. The design of this study was that of a quasi-experimental randomized two group study with a level of evidence of III in which the control consisted of CB alone and the treatment consisted of CB with inhaled IPA. The authors used convenience sampling in a community hospital's outpatient surgery center in the United States. A power analysis was conducted and determined the need for 100

participants with 50 participants in each group to yield results of statistical significance of $p = 0.05$. In the end, 41 patients were included in both control and treatment groups. Inclusion criteria included being a female patient between of 18 and 60 years old, and having outpatient laparoscopic surgery under general anesthesia with an endotracheal tube or laryngeal mask airway. Exclusion criteria for this study included having nausea prior to administration of anesthesia, having allergies to IPA, the inability to breathe effectively through the nose, not being able to read or speak English and finally, having documented Alzheimer's disease or dementia and/or not being able to provide informed consent. Patients were instructed on how to slowly inhale through the nose for three breaths and exhale through the mouths and on how to use the verbal numeric nausea intensity scale from zero to 10 and upon the first presentation of nausea in the PACU. The participants were randomly assigned to control group in odd calendar months and the treatment group assigned to even calendar months. The participants were then asked to rate their nausea on the scale from zero to 10 and were guided through the CB exercises. The treatment group had a gauze pad with IPA on it placed below their nose for inhalation. The participants were again asked to rate their nausea two minutes later and if symptoms remained, the participants were able to choose between repeating the same procedure or using rescue antiemetics. Scores on the verbal numeric nausea scale were again collected three minutes later if participants repeated the procedure and participants were once again allowed to choose between repeating the procedure and rescue antiemetics if symptoms continued to persist. The authors did not disclose how data analysis was conducted which was a major limitation of the study. The authors found that the data between groups regarding time spent in surgery, type of surgery, history of nausea or vomiting, and amount of fluids were similar except for data regarding age which was significantly higher in the treatment group ($p = 0.03$) and history of smoking which

was significantly higher in the control group (p =0.04). Similarly to how nausea scores decreased significantly over time in both treatment and control groups ($p < 0.001$), the number of participants requesting rescue antiemetic medication did not differ significantly from treatment to control groups at two minutes ($p = 0.78$), at five minutes ($p = 0.48$), or overall ($p = 0.18$). Additionally, there were no significant differences in nausea scores between the intervention and control groups ($p = 0.09$). One limitation of this study was that because many of the study participants received a variety of antiemetic medication both preoperatively and/or intraoperatively, they did not experience PON and were not included in control and treatment groups therefore limiting the size of the study. Additionally, the subjects were not blinded and therefore it was a quasi-experimental study with a level of evidence of III instead of a randomized controlled trial with a level of evidence of II. Though the results need to be interpreted with caution, the authors conclude that CB can be used to help control PON and should be taught to patients as a first response to PON due to the cost effective nature of the intervention with no side effects. The authors also assert that more research is needed to definitively conclude that aromatherapy is no more effective than controlled breathing at reducing PON. Because this study was conducted in a non-specialized community hospital with patients undergoing a variety of laparoscopic procedures, the results may be generalizable to larger populations or those undergoing surgeries of similar invasiveness as laparoscopies. Despite the generalizability of this study, the results may not be of high quality and therefore should be interpreted with caution.

Comparison of Inhalation of Isopropyl Alcohol vs Promethazine in the Treatment of Postoperative Nausea and Vomiting (PONV) in Patients Identified as at High Risk for Developing PONV

Pellegrini, DeLoge, Bennet and Kelly (2009) disclose that for patients who are identified as having a high risk for developing PONV, prophylactic ondansetron is widely used though it is only 25% effective. As a result of the ineffectiveness of ondansetron, promethazine is often used to treat breakthrough PONV. Promethazine can cause unpleasant symptoms such as dry mouth and sedation and even dangerous side effects such as hypotension. Additionally, providers often prescribe oral or suppository forms of promethazine for outpatients and who are often hesitant towards these forms of mediations due to the presence of nausea and social stigmas. Because of the issues associated with promethazine, the research team conducted a study to determine if 70% IPA aromatherapy was more beneficial than intravenous (IV) promethazine at treating breakthrough PONV in patients identified as high risk who had previously received prophylactic ondansetron. The study design was that of a randomized controlled trial with a level of evidence of II. A power analysis was conducted and determined the need for 40 participants in each group, however after factoring in a possible attrition rate of 20%, the sample size to increase to 96 with 48 participants in each group. The researchers used convenience sampling and recruited a total of 85 participants with 43 in IPA aromatherapy intervention group and 42 in the promethazine control group randomly assigned via computer generation. Inclusion criteria for this study included being scheduled for a surgery with anesthesia lasting more than one hour, and having at least two of the four risk factors for PONV including being of female gender, a history of PONV, a history of motion sickness and/or being a nonsmoker. Exclusion criteria for this study included, having recent upper respiratory infections, being pregnant, being unable to

breathe through the nose, using psychoactive or antiemetic drugs within the past 24 hours, having a body mass index (BMI) of 35 kg/m^2 or more, being allergic to metoclopramide, promethazine, ondansetron or IPA, or requiring the need for hospitalization not related to PONV. The study was conducted in the PACU, the same-day surgery unit (SDSU), and following discharge at home in the United States. All participants received 4 mg of IV ondansetron prophylactically 15 to 30 minutes before being extubated. The control group received 12.5 to 25 mg IV promethazine in the PACU and SDSU or used self-administered promethazine suppositories after discharge, and the intervention group received 70% inhaled IPA aromatherapy as a treatment. After researchers received informed consent, the participants preoperatively rated their baseline nausea on a visual numeric rating scale (VNRS) from zero to 10 with zero being "no nausea" and 10 being "worst imaginable nausea" (Pellegrini et al., 2009). Upon arrival in PACU and SDSU, VNRS scores were again recorded for nausea with each episodes of nausea being at least one minute from the last at the first patient complaint of nausea. VNRS scores were again recorded after the first complaint every five minutes for the first 30 minutes, and every 15 minutes following that for the following 75 minutes or discharge, whichever came sooner. The control group in the PACU and SDSU received IV promethazine upon first patient complaint of nausea with the ability to repeat treatment after 30 minutes up to a total of 50 mg per patient. If the initial promethazine administration was sufficient to relieve PONV symptoms, patients could receive 10 mg IV metoclopramide every 15 minutes with a maximum does being 30 mg per patient. Upon discharge, the patients were instructed to use a 25 mg promethazine suppository every six hours as needed at home. In the intervention group, the participants each received 70% IPA pads in paper coverings and were then instructed to remove the cover, fold the pad, hold the pad 0.5 inches away from the nares and to take three deep

breaths through the nose before throwing away the pad both in the PACU, SDSU and post discharge. This protocol was repeated as needed up to three times. Intervention group patients also were instructed on the use of 25 mg promethazine suppositories if their PONV symptoms were not resolved with IPA aromatherapy. Patients in both groups received paperwork to document their VNRS scales at home and instructions on when to collect this information in regard to administration of treatments. The participants then reported their VNRS scales on telephone calls along with data regarding their satisfaction of their specific antiemetic therapy on a scale of one to five with one being "totally dissatisfied" and five being "totally satisfied" (Pellegrini et al., 2009). SPSS software was used to statistically analyze the data, Chi-squared tests and Pearson correlations were used to analyze frequencies, and VNRS scores were analyzed with *t* tests with $p \leq 0.05$ considered to be statistically significant. There were no significant differences found in surgery times or demographic data save for the fact that participants in the intervention group received significantly more nitrous oxide ($p = 0.049$) than the control group. Follow up statistical analyses were conducted and the amount of nitrous oxide administered did not show statistically significant effects in increasing risk of PONV. The authors found no significant differences between control and intervention group in incidence of nausea until discharge. The intervention group experienced a faster decline in VNRS scores of nausea than control group in the, SDSU ($p = 0.032$), PACU ($p = 0.045$) and at home ($p = 0.017$). Significantly more participants in the control group used their promethazine suppository as a rescue antiemetic at home compared to the number who used inhaled IPA at home ($p = 0.039$). The authors admit that there were limitations to their study including that the number of participants were limited because the methods of data collection were intensive and time consuming and therefore limited the number of participants to one to two per day. Additionally,

the data regarding rescue antiemetic medication at home, specifically promethazine, may be influenced as there may be a social stigma concerning rectal suppositories. In the end, the authors conclude that participants in the intervention group experienced less side effects from IPA than those in control group from promethazine. Additionally, IPA is as effective as promethazine for treatment of PONV in patients identified as being high risk for developing PONV and is more cost effective, easy to administer and works faster than promethazine. Despite the relatively small sample size, the study was conducted with a high level of evidence, in a broad population and yielded results of statistically significant indicating generalizability and applicability of results.

Aromatherapy for Treatment of Postoperative Nausea and Vomiting (Review)

Hines, Steels, Chang and Gibbons (2018) updated a systematic review with a level of evidence of I originally published in 2012 under The Cochrane Collaboration. The purpose of the review was to establish both the safety and efficacy of aromatherapy compared to standard pharmacotherapy for PONV severity and duration in both children and adults. A variety of databases were searched including MEDLINE, CINAHL EmBase, CENTRAL, PubMed, ISI Web of Science, Informit and LILACS for articles published until March of 2017. Search criteria included all clinical controlled trials (CCTs) and randomized controlled trials (RCTs) in which aromatherapy was used a treatment for PONV with primary outcomes being PONV duration and severity and secondary outcomes being use of rescue antiemetics, adverse reactions and patients' satisfaction. Two of the four authors read titles and abstracts of articles to determine relevance of full text articles and translated articles that were potentially relevant and not in English. Three authors compared those articles with inclusion criteria via a standardized checklist for the review. Following the review for inclusion criteria, two authors extracted data using Plot

Digitizer software. Risk of bias was assessed by two authors with a third author settling any disputes using a Cochrane tool for characteristics including blinding, randomization, allocation concealment, selective reporting and incomplete data. In total, 16 studies were included in the review including 5 CCTs and 11 RCTs with a total of 1036 participants. Articles were assessed for quality using the GRADE approach and the studies included were found range between very low quality and moderate quality. A risk ratio (RR) was used to compare dichotomous data with 95% confidence intervals (CI) and a standardized mean difference (SMD) was used to analyze continuous variables. The authors found that compared to a placebo, aromatherapy was not effective in reducing the severity of PON ($p = 0.28$) or was significantly related to the likelihood of absence of PON at the end of the treatment period ($p = 0.33$). Additionally, peppermint aromatherapy compared to placebo was not effective at reducing PON ($p = 0.59$). Compared to the placebo, those in the aromatherapy group were significantly less likely to need to use rescue antiemetic medications ($p = 0.04$). IPA aromatherapy was found to be beneficial as compared to standard antiemetic therapy as the IPA aromatherapy group showed significantly quicker times to reach 50% reduction in PON ($p < 0.00001$) Also the IPA aromatherapy group patients were significantly less likely to require rescue antiemetic medication than the control group patients ($p = 0.04$). Although IPA aromatherapy reduced the time to reach a reduction in PON, it did not produce significantly fewer instances of need for rescue antiemetic compared to standard antiemetics ($p = 0.11$). In conclusion, the authors assert that low quality evidence suggests that those using aromatherapy may require less rescue antiemetic therapy and may have a similar effect as placebo on eliminating nausea. Because the results of this study are based off of quality including very low quality data, the results may not be accurate or generalizable and there

remains need for further studies of high quality evidence regarding the use of aromatherapy for prevention and treatment of PONV.

Acupuncture of Pericardium 6 Acupressure Point

Comparison Between Effects of Acupuncture and Metoclopramide on Postoperative Nausea and Vomiting after Gynaecological Laparoscopy: A Randomized Controlled Trial

Albooghobeish et al. (2017) assert that common drugs used to alleviated PONV such as metoclopramide and ondansetron often have significant side effects including hypotension, drowsiness and extrapyramidal symptoms (EPS) and an alternative treatment of acupoint stimulation has minor side-effects and is minimally invasive. Despite these facts, there has been little research comparing the effects of traditional pharmacotherapy with acupuncture of point P6 in relation to PONV. This double-blinded, randomized controlled trial with a level of evidence of II was conducted in order to compare the effect acupuncture and metoclopramide for PONV in gynecologic laparoscopic surgeries. A power analysis was conducted and determined the need for 36 participants in each of the three study groups in order to yield results of statistical significance. The control group received IV normal saline, the intervention group received IV metoclopramide, and a second intervention group received P6 acupuncture. The study was conducted in a general hospital in Ahvaz, Iran, with patients who were selected through convenience sampling. In the end, there were a total of 41 participants in the control group, 40 participants in the P6 acupuncture group and 41 participants in the metoclopramide group who were randomized via computer generation. Inclusion criteria for this study included being a patient undergoing gynecologic laparotomy, being of ASA status I, and being between 19 and 46 years or age. Exclusion criteria for this study included having a history of smoking, having a history motion sickness, having a history of ear or gastrointestinal disorders that can cause

vomiting and nausea, having a BMI of 30 kg/m^2 or higher, taking any antihistamine or antiemetic medication within 24 hours of surgery, experiencing nausea and vomiting a week or less before surgery, taking drugs that may cause EPS and having any scarring or infections at the site of acupuncture. Acupuncture was done with a sterile needle with a diameter of 0.25 mm and a length of 25 mm. The needle was inserted at a depth of five to seven mm at the P6 acupoint directly after anesthesia induction. The need was removed before extubation and before transfer of patient to recovery. Patients in the metoclopramide group received 0.2 mg/kg IV metoclopramide directly after anesthesia induction. The control group received 1.0 mL of IV normal saline directly after anesthesia induction with the administration of fluids terminated before extubation. The examiners of PONV were anesthesia assistants that were different from anyone who completed the intervention and therefore were not biased in their examination and data collection of PONV symptoms. All patients were given 10 mg IV metoclopramide if they vomited and all received a suppository of 100 mg sodium diclofenac for analgesia. Data on vomiting and nausea occurrences were collected in the form of observation by the anesthesia assistant and questioning of the patient both one and two hours postoperatively. The demographic data was analyzed with mean, standard deviation and descriptive statistics. The incidence of nausea and vomiting were reported as both percentages and frequencies. Comparative data was analyzed with Chi-squared and Fisher's tests with a statistical significance set at $p \leq 0.05$. The authors found no statistically significant differences in demographic groups but did find that the incidence of PON and postoperative vomiting (POV) one and two hours after surgery was lowest for the acupuncture group. Additionally, one hour after surgery, the acupuncture group experienced significantly lower incidences of PON compared to metoclopramide group ($p = 0.027$). The acupuncture group compared to control group

experienced significantly fewer episodes of PON one hour after surgery ($p = 0.015$), two hours after surgery ($p = 0.002$), and POV two hours after surgery ($p = 0.011$). The metoclopramide group compared to control group experienced significantly fewer incidences of POV two hours after surgery ($p = 0.046$). The authors concluded that acupuncture of P6 is more effective than no intervention for reducing PONV and may be more effective than metoclopramide intervention for reducing PONV. Additionally, P6 acupuncture reduces the need for antiemetic medication and PONV in gynecologic laparoscopies. The authors concede that their short follow up time may have confused the results of the study and that studies following late onset PONV may be necessary to better generalize the results. Though this study was conducted very well, it may not be generalizable to a larger population as it was conducted with a very specific population of women receiving gynecological laparoscopic operations.

Comparison of the Wrist Acupuncture Point P6 with Pharmacologic Management to Prevent Postoperative Nausea and Vomiting in Patients Under Laparotomy: A Double Blind Study

Bakhshaei, Khoshraftar, Shoja and Mehrabi (2018) note that when taking into account the cost-benefit analysis of alternative therapies to manage and prevent PONV, alternative therapies are becoming more enticing compared to traditional pharmacotherapies. In this double- blind randomized control trial with a level of evidence of II, the authors set out to determine the effectiveness of wrist acupuncture compared to traditional medication for management of PONV in patients undergoing laparotomies. The authors did not mention use of power analysis to determine sample size, however it is stated that 100 participants were recruited through convenience sampling to yield a total of 50 participants in both the control of standardized medications and intervention group of wrist acupuncture. Inclusion criteria for this study

included being between 18 and 70 years of age, being a candidate for an elective laparotomy, being ASA status I or II, having no history of PONV, being under general anesthesia, not using antiemetics within the 24 hours prior to surgery, and the signing of an informed consent. Exclusion criteria for this study included dependencies on drugs or alcohol, the use of opium, the presence of wounds or scarring at acupuncture site, not being 18 to 70 years old, having a history of psychological or neurological disorders, undergoing surgery lasting longer than two hours, having a history of disorders precipitating nausea and vomiting, being pregnant, vomiting or becoming nauseous 24 hours prior to surgery, those refusing acupuncture, or those receiving chemotherapy in the past seven days. All 100 participants were randomized with computer generated "balanced block randomization" (Bakhshaei et al., 2018). The control group received a combination of metoclopramide with dexamethasone with unknown doses or timings with the participants being blinded to the treatment. Those in the acupuncture group perceived bilateral P6 acupuncture 30 minutes before the conclusion of surgery and were blinded to the treatment as well. The site of acupuncture was cleaned with 75% IPA, disposable sterile needles with a diameter of 0.25 mm and length of 25 mm were inserted perpendicularly to the skin until they reached a depth of 10 mm at the P6 acupoints. Upon insertion, the needles were pushed downward, lifted upward and twirled. An independent nurse collected data regarding demographics, duration of anesthesia, duration of surgery, preoperative data and duration of endotracheal intubation. An independent observer blinded to the interventions recorded postoperative data for the 24 hours following surgery including satisfaction of patient with PONV management, need for and use of rescue antiemetics, episodes of nausea with the patient reporting on a VAS from zero to 10 with zero being "no nausea at all" and 10 being "worst imaginable nausea" and episodes of vomiting assessed by the observer after reporting by the

patient (Bakhshaei et al., 2018). Data analysis was conducted with quantitative variables analyzed in the form of percentages and frequencies, continuous variables analyzed using *t* tests, and categorical variables analyzed with Chi-squared and Fisher's tests. Statistical significance was determined to be $p \leq 0.05$. The authors found that mean recovery times were not significantly different between the control and intervention groups nor was prevalence of PONV. The authors concluded that P6 wrist acupuncture could be of similar effectiveness to metoclopramide with dexamethasone for prevention of PONV and that P6 wrist acupuncture may be more desirable than pharmacologic antiemetic medication due to the side effects and cost associated with the medications. While these results are clinically significant, it is important to note that because the researchers did not disclose the specific intervention information regarding metoclopramide and dexamethasone pharmacotherapy, the readers do not have a clear understanding as to what medication regimen P6 acupuncture is similar or comparable to. Additionally, while the findings presented in this study are consistent with findings published in other articles, the interventions were tested on a relatively small group of patients undergoing elective laparotomies and may not be generalizable to larger populations.

The Effect of Acupuncture on Postoperative Nausea and Vomiting after Pediatric Tonsillectomy: A Meta-Analysis and Systematic Review

Shin et al. (2016) published a systematic review and meta-analysis with a level of evidence of I in *The Laryngoscope,* the official publication of The American Laryngological, Rhinological and Otological Society. The purpose of this review was to determine the antiemetic efficacy of acupuncture following pediatric tonsillectomies. A total of seven authors published the study with smaller numbers of researchers conducting different portions of the review. For example, two of the researchers independently searched databases including EmBase,

MEDLINE, and Cochrane databases for articles including keywords “tonsillectomy,” “child,” “acupuncture,” “acupuncture therapy,” and “vomiting” that were published before July of 2015. To be included in the review articles had to be full length and original, and either a retrospective or prospective trial or a RCT. Exclusion criteria for the articles in this review included not having a control group, being published in any language other than English, inclusion of adults in the sample, having 10 or less cases of PONV, or if the study was not related to tonsillectomies. The authors screened the titles and abstracts of articles to determine relevance and compliance with inclusion and exclusion criteria and yielded a total of eight studies. The studies included in the review included four RCTs, three prospective cohort studies, and one pilot study yielding a total of 800 subjects with 406 subjects in the control group of no treatment or classic antiemetic treatment. and 394 subjects included in the acupuncture intervention group. All acupuncture therapies included in this study included either bilateral or unilateral acupuncture of the P6 acupoint. RRs were used to represent effect size with a 95% CI, standard errors were calculated, and a Cochrane Review Manager was used to analyze and display data statistically. Subgroup analyses were conducted regarding both methodology and modality. Publication bias was analyzed and represented on a funnel plot, and if found, was corrected with “Duval’s trim-and-fill method” (Shin et al., 2016). A sub method for correcting publication bias was used on one cohort study that was unpublished at the time the review was conducted. Though the authors do not state how the articles were assessed for quality, they do state that the eligible studies ranged from high quality to moderate quality. The authors found that the incidence of PONV was significantly reduced for acupuncture interventions compared to control by 23% with a relative risk ratio of 0.77 ($p < 0.05$). Additionally, electrostimulation interventions had a significantly lower RR than that of traditional acupuncture (0.59 compared to 0.87) ($p <$

0.05). Finally, the RR from randomized controlled trials was lower than that of the prospective cohort studies (0.74 compared to 0.83) though it was not statistically significant. The researchers admit that there was an outlier in one study, though the omission of the outlier did not alter the results of the risk ratio (0.787 compared to 0.77) and the outlier may have occurred due to the specific method of electrostimulation used which may have had a greater effect on PONV than the other studies. Shin et al. (2016) conclude that acupuncture is an effective form of alternative antiemetic therapy to reduce PONV after pediatric tonsillectomies. While the researchers do not state if their results are consistent with previous findings, they appear confident that with further research, acupuncture could improve patient outcomes and experiences.

The Effectiveness of Acupuncture in Prevention and Treatment of Postoperative Nausea and Vomiting – A Systematic Review and Meta-Analysis

Cheong, Zhang, Huang and Zhang (2013) conducted a systematic review and meta-analysis with a level of evidence of I originally published by PLoS ONE in order to determine the efficacy of multiple acupuncture treatments and of acupoint selections on treating and preventing PONV. While acupoint selection and type of acupuncture were the primary outcomes being looked at, secondary outcomes included side effects, use of rescue antiemetics, optimal timing of intervention, and techniques used in interventions. The researchers searched EBSCO, Cochrane Controlled Trials Registry, OVID, PubMed, Wanfangdata and CNKI for terms including “nausea and vomiting,” “postoperative,” “acupoints,” “acupressure,” “acupuncture,” “electroacustimulation,” “transcutaneous electric nerve stimulation,” “electro-acupuncture,” “electrical acupoint stimulation,” “electrical acustimulation,” “auricular acupuncture,” “sticking therapy,” “warm need therapy,” “moxibustion,” and “moxa” published up to July of 2013. Search criteria included RCTs, any form of acupuncture, participants who underwent some kind

of surgery, and results collected form publications between 1986 and 2013. Exclusion criteria for this review included trials that were not randomized, patients who experienced nausea and vomiting preoperatively, those with chronic or co-existing conditions, patients who used antiemetics preoperatively, articles not originally published in Chinese or English, and articles that did not include detailed protocol descriptions. The evaluation of the articles for inclusion was performed by two of the four authors with a third author resolving any discrepancies or disputes. Within this review, the control was considered to be sham interventions, standard care protocols, counseling and/or medication while the intervention was considered to be any type of acupuncture including acupressure, manual acupuncture, electrical acupoint stimulation, and combinations of techniques. A total of 30 RCTs were included in the review with a total of 1,276 participants in the control group and 1,258 participants included in the acupuncture intervention group. Data was compiled in a Microsoft Excel document and analyzed with a fixed-effects model, and RRs with 95% Cis. $p < 0.05$ was considered to be statistically significant and risk of bias was assessed with funnel plots. Included studies were assessed for quality using the GRADE method scoring each article as high quality, moderate quality, low quality or very low quality. The researchers found that PC6 acupuncture significantly reduced overall incidences of PON zero to 24 hours ($p = 0.002$) but not early PON within zero to six hours. Similarly, PC6 acupuncture significantly reduced incidences of early POV zero to six hours ($p = 0.003$) but not for overall vomiting zero to 24 hours. PC6 acupressure was found to significantly reduce incidences of PON zero to 24 hours ($p = 0.001$) and POV zero to 24 hours ($p = 0.000$) compared to the sham intervention groups. Additionally, PC6 electro-acupoint stimulation significantly reduced incidences of PON zero to 24 hours ($p < 0.000$) and POV zero to 24 hours ($p < 0.000$) compared to the sham intervention group. Finally, PC6 stimulation combined with other

acupoints significantly reduced incidences of PONV zero to 24 hours ($p = 0.001$) POV zero to 24 hours ($p = 0.000$) and PON zero to 24 hours ($p = 0.000$) compared to the control groups. The authors site several articles and previous reviews that produced similar results regarding the efficacy of P6 acupuncture for prevention of PONV. Out of the studies regarding P6 acupoint included in this study, four were of high quality, nine were of moderate quality and three were of low quality. Though the studies regarding P6 were solely focused on prevention and not treatment of PONV, the timing of the acupuncture interventions varied, and the durations of the acupuncture interventions varied, there is still strong evidence that acupuncture of the P6 acupoint can effectively prevent PONV. P6 acupuncture is both safe and cost effective, and the results of this study are clinically relevant and applicable for both treating and preventing PONV.

Stimulation of the Wrist Acupuncture Point PC6 for Preventing Postoperative Nausea and Vomiting (Review)

Lee, Chan and Fan (2015) updated a systematic review with a level of evidence of I originally published in 2004 for the Cochrane Collaboration. The purpose of the review was to determine both the safety and efficacy of stimulation of the P6 acupoint either in combination with antiemetic drugs or alone compared to antiemetic drugs or sham interventions in the prevention of PONV in surgery patients. Databases searched included MEDLINE, ISI Web of Science, EmBase, Cochrane Central Register of Controlled Trials, World Health Organization Clinical Trials Registry and ClinicalTrials.gov. Search terms included “nausea and vomiting,” “postoperative complications,” “acupuncture therapy,” “acupuncture,” “transcutaneous eclectic nerve stimulation,” “electro-acupuncture,” and “acupressure” (Lee et al., 2015). Search criteria included randomized trials involving P6 acupoint stimulation in comparison with medications or sham treatments, or combination of medication with P6 stimulation compared to medications

alone for PONV prevention. The primary outcome of this review was PONV incidence and secondary outcomes were adverse effects of treatment and need for rescue antiemetic medications. Titles and abstracts of all studies accumulated in the search were screened for compliance with inclusion criteria by two researchers with a third settling disputes or discrepancies. Risk for bias was assessed using Cochrane guidelines from low risk of bias to high risk of bias and articles were assessed for quality using the GRADE approach ranging from high to very low qualities of studies. In total, 59 RCTs were included in this review with a total of 7,667 patients in all studies. A random effects model was used to analyze the data and reported as RRs with a 95% CI. Trial sequential analysis (TSA) was conducted to inform the required size of information for a 30% reduction of RR. The authors found that P6 acupoint stimulation significantly reduced the incidence of PON, POV and need for rescue antiemetic drugs. It was also found that P6 acupoint stimulation did not significantly reduce the incidence of PON, POV or need for rescue antiemetic drugs when compared to six different antiemetic drugs. Combination of antiemetic drugs with P6 acupoint stimulation reduced POV and did not reduce PON or the need for rescue antiemetic drugs. The P6 acupoint stimulation group in combination with antiemetic drug therapy compared to antiemetic drug therapy alone needed less rescue antiemetic drugs. While in one study a participant was not blinded, in two studies the providers were not blinded, in three studies the assessors were not blinded, in three studies there were attrition rates and the interventions included were not solely limited to P6 acupoints, the quality of evidence is moderate. The authors conclude that, P6 acupoint stimulation is a worthwhile intervention for those at high risk for developing PONV due to the minor adverse effects and may be considered an alternative antiemetic treatment for certain patients. This study is clinically applicable, generalizable, and it is clear that the information from this review can both improve

experiences of care as well as the outcomes of patients undergoing surgery and experiencing PONV.

Supplemental Inspired Oxygen

Effects of High Intraoperative Inspired Oxygen on Postoperative Nausea and Vomiting in Gynecologic Laparoscopic Surgery

Simurina et al. (2010) assert that there is very little data regarding the use of 0.5 FIO_2 on early and late postoperative PONV. Because of this, the authors set out to test their hypothesis that high intraoperative FIO_2 of 0.5 and 0.8 compared to the 0.3 FIO_2 used routinely would reduce PONV in the first 24 hours in women recovering from elective gynecologic laparoscopies under general anesthesia. This study was a RCT with a level of evidence of II. The settings for this study was the PACU and gynecologic floor of a general hospital in Zadar, Croatia. A power analysis was conducted and determined the need for 37 participants in each group to yield "80% power for detecting a 50% reduction in the frequency of PONV" and an α of 0.05 (Simurina et al., 2010). Convenience sampling was used and a total of 36 patients were included in each of the three groups; one receiving FIO_2 of 0.3, one receiving FIO_2 of 0.5 and one receiving FIO_2 of 0.8. Inclusion criteria was defined as patients of ASA class I or II, provision of informed consent, being an adult, and receiving elective gynecological laparoscopies. Exclusion criteria for this study included having a BMI of 30 kg/m^2 or more, being pregnant, breastfeeding, having a pulmonary disease, having a disease that could impair gastric motility, having known hypersensitivities to medications, using antiemetics, hormones, steroids or psychotropic drugs within three days of surgery, having a history of migraines, having renal impair, having a history of vestibular diseases, patients with irregular menstrual cycles, patients with injury to the central nervous system or having dependence on alcohol or opioids. Additionally, participants were

excluded from the study after enrollment if they developed intraoperative complications such as severe hypotension, drug hypersensitivities, excessive blood loss, intubation difficulties, or preoperative hypoxia those who developed complications postoperatively. A total of 40 participants were randomized to each of the three treatment groups via randomized computer generation, however four participants were excluded from each group due to a variety of reasons. All study participants were given 7.5 mg oral midazolam one hour preoperatively, did not receive prophylactic antiemetics, were given the same anesthesia, were all ventilated with FIO_2 1.0 for three minutes prior to being intubated, were given 10 mL/kg/hr of IV crystalloids and were ventilated with 0.3, 0.5, or 0.8 FIO_2. Data was collected on frequency of use of rescue antiemetics, PON and POV at two hours and 24 hours postoperatively. Nurses trained on the study and blinded to the interventions of each patient used a VAS to analyze the PON and pain of patients from zero to 100 with zero being "no pain/nausea" and 100 being "maximal pain/nausea" (Simurina et al., 2010). The highest score reported in the first two hours and the highest score in the two to 24-hour time period were used for analysis of data. Quantitative data including episodes of vomiting, VAS scores, risk scores and demographic data were analyzed with ANOVA. Categorical data was analyzed using Chi-squared tests and *t* tests. All confidence intervals were 95%, and statistical significance was considered to be $p < 0.05$. The authors found that compared to 30% oxygen, patients receiving 80% oxygen experienced significantly fewer episodes of early POV ($p = 0.0028$). Additionally, patients with supplemental oxygen of either 50% or 80% experienced fewer episodes of vomiting ($p = 0.010$). The authors conclude that high inspired oxygen does not reduce PONV but does reduce early POV and that high inspired oxygen has limited use and should not be recommended for routine PONV prevention. The authors admit that because the number of participants was lower than the power analysis

indicated there should be, there may be risk of type 1 statistical error which results in a false positive. Because of the small sample size, the results must be interpreted with caution and may not have clinical applicability.

Effect of Supplemental Oxygen 80 % on Post-Tonsillectomy Nausea and Vomiting: A Randomized Controlled Trial

Izadi, Delavar, Yarmohammadi, Daneshmandan, and Sadrameli (2016) state that supplemental oxygen has been shown to prevent PONV however there is no consensus on what types of surgeries and what amounts of oxygen this is true for. Because of this lack of consensus, the authors conducted a randomized controlled trial with a level of evidence of II to test the hypothesis that PONV in pediatric patients undergoing tonsillectomies can be reduced in the first 24 hours postoperatively through use of 80% supplemental oxygen. The setting for this study was a hospital in Tehran, Iran. A power analysis was conducted and determined the need for a sample size of 46 participants in each group. In order to allow for small amounts of attrition, 51 participants were recruited through convenience sampling and were randomized using computer based software to each group. Patients were included in the study if they were between five and 15 years old, were undergoing tonsillectomies and their parents provided informed consent. Exclusion criteria for this study included having any comorbidities that may have influenced PONV such as gastroesophageal reflux disease (GERD), anemia, diabetes mellitus (DM), immune deficiencies or kidney disease, anyone using antiemetics or those with craniofacial abnormalities. Participants were further excluded if they were difficult to intubate, developed allergies to the drugs being used, or if they needed additional analgesia or opioids. All participants received the same method of anesthesia, the same preoperative medications, the same IV solutions, and same methods of intubation with the only difference in treatment being

the amount of inspired oxygen either intraoperatively with routine 30% oxygen or high inspired oxygen of 80%. Three trained nurses who were blinded to the amount of intraoperative oxygen collected data on the frequency of PONV zero to two hours postoperatively, between hours two and six postoperatively, and between six and 24 hours postoperatively. SPSS software was used to analyze the data with results considered to be statistically significant at $p < 0.05$. The authors found that the incidence of nausea and vomiting in the first two hours following surgery was significantly higher than incidences in two to six hours or six to 24 in the 30% O2 control group ($p = 0.003$). Additionally, there are were no significant differences in incidence of nausea and vomiting between zero to two hours, two to six hours and six to 24 hours after surgery in the 80% O_2 intervention group. The authors conclude that 80% supplemental oxygen has a positive effect on PONV compared to 30% in children undergoing tonsillectomy especially in the first two hours postoperatively. The authors also admit that the results of this study conflict with a meta-analysis conducted by Orhan-Sungur et al. (2008), and other RCTs. The authors therefore suggest that there is need for further research regarding the effect of supplemental oxygen on PONV. Additionally, the authors suggest that beneficial effect of supplemental oxygen in on PONV in this study may be due to lowering serotonin levels in the pharynx. Because the results are not consistent with other findings, and because this intervention was conducted on a specific group of patients undergoing pediatric tonsillectomies, the results may not be valid or generalizable to larger populations.

Supplemental Oxygen Does Not Prevent Postoperative Nausea and Vomiting after Gynecological Laparoscopy

McKeen, Arellano and O'Connell (2009) conducted a double blinded, randomized controlled trial with a level of evidence of II. The set out to test the hypothesis that high

intraoperative 80% oxygen compared to 30% oxygen reduces PONV in the first 24 hours following ambulatory gynecological laparoscopies under one hour in duration. This study was conducted in Halifax, Canada both in a Health Center and at patients' homes following discharge. A power analysis was conducted and determined the need for 138 participants in each group. The researchers therefore enrolled 152 women into each group to allow for possible drop out. Through convenience sampling, a total of 145 women were included in the control group receiving standard 30% oxygen, and 147 women were included in the intervention group receiving 80% oxygen. In the control group six participants did not receive the intervention and data seven participants as not included for violations of protocol. In the intervention group two participants did not receive the intervention and data from five participants was not included for violations of protocol. Inclusion criteria for this study included being of ASA status I or II, and undergoing "ambulatory laparoscopic tubal ligation" (McKeen et al., 2009). Exclusion criteria for this study included having a BMI of 37 kg/m^2 or more, anyone currently breastfeeding, having DM, requesting benzodiazepines preoperatively, having gastroparesis, using antiemetic for nausea and vomiting, using cannabis or opioids, having known substance abuse issues in the past six months, having a history of PONV that lasted over 24 hours or anyone requiring hospital admission postoperatively. After endotracheal intubation, participants received either 30% routine oxygen or 80% supplemental oxygen determined by computer randomization. The interventions were carried out by an anesthesiologist not blinded to the interventions while everyone else on the medical team and the patient were blinded to the intervention. Following anesthesia, all patients received O_2 at two mL/min delivered via nasal cannula with supplemental oxygen given to maintain SpO_2 above 92%. If patients experienced vomiting or nausea for than 15 minutes or more, four to eight mg IV ondansetron was given as an antiemetic. If PONV was

still unresolved the patients received either IV dexamethasone and/or IV diphenhydrinate. An observer blinded to the interventions recorded episodes of nausea and vomiting every 30 minutes upon patient entry in PACU until time of discharge on a four-point scale from "none" to "severe" (McKeen et al., 2009). Additionally, at home patients recorded their episodes of vomiting and severity of nausea for the first 24 postoperative hours and reported them to observers via phone interviews. The primary outcome being analyzed was the incidence of PONV in the first 24 hours and secondary outcomes being analyzed included doses of antiemetics taken postoperatively, postoperative time until admission of oral antiemetic, the amount of time it took to discharge the patient, and the PACU and at home scores regarding nausea and vomiting. Dichotomous variables were analyzed using Chi-squared tests, maximum nausea and vomiting scores were analyzed using the *U* test, and factors that could be potentially confounding were analyzed with *t* tests and Chi-squared tests. Results were presented as odds ratios (ORs) with 95% CI, standard deviations, means, ratios and medians with statistical significance set at $p < 0.05$. While the anesthesia duration was only longer for the supplemental oxygen intervention group, it was statistically significant ($p = 0.02$). The authors found that there were no statistically significant differences between the control and intervention group in early, late, pre-discharge, post-discharge or primary outcome PONV. Additionally, statistically significant predictors of PONV included previous history of PONV ($p = 0.02$), those of younger age ($p = 0.005$), surgery time ($p = 0.04$), in hospital morphine equivalents ($p < 0.0001$) and total morphine equivalents 24 hours post-discharge ($p = 0.002$). The authors conclude that there is no clear benefit to using 80% O2 compared to 30% O_2 to reduce the incidence of PONV in patients undergoing laparoscopic gynecological surgery. Additionally, the authors assert that to better manage PONV, there need to be better methods of identifying the patients who are at risk for developing

PONV as well as better methods of decreasing postoperative opioid use. The results of this study are limited to a fairly specific population of patients undergoing laparoscopic tubal ligations and therefore may not be generalizable to the larger population. The results of this study also do not provide evidence for use of supplemental oxygen and therefore may not be clinically relevant for prevention of PONV.

Effect of Intraoperative High Inspired Oxygen Fraction on Surgical Site Infection, Postoperative Nausea and Vomiting, and Pulmonary Function: Systematic Review and Meta-Analysis of Randomized Controlled Trials

Hovaguimian, Lysakowski, Elia, and Tramèr (2013) conducted a systematic review and meta-analysis with a level of evidence of I in order to determine the benefit of high inspired oxygen on surgical site infection (SSI) and PONV and determine the potential complications of high inspired oxygen on pulmonary function. Multiple databases were searched for RCTs including MEDLINE, Central Databases and EmBase for terms including "oxygen," "anesthesia," "supplemental" and "and/or" for articles published up until the searchers were conducted in September of 2012 (Hovaguimian et al., 2013). Inclusion criteria included RCTs regarding adult patients undergoing surgery of any kind under general anesthesia, articles comparing high FIO_2 of 80-100% to low or normal FIO_2 of 30-40% and having patients that exhibited at least one of the three outcomes explored; PONV, SSI, or postoperative pulmonary outcomes. Articles were excluded if they were animal studies, were only abstracts, if high FIO_2 was delivered outside of the general anesthesia, if the patients had one-lung surgery, of if supplemental oxygen was delivered only postoperatively and not with the general anesthesia. One researcher reviewed articles for inclusion and exclusion criteria with a second researcher independently checking the first and a third resolving disputes or discrepancies between the other

two. A total of 22 RCTs were included in this review with 11 of them regarding PONV. One author alone extracted data from selected articles with a second author checking the data and a third resolving disputes or discrepancies between the other two. One author assessed articles for quality using an Oxford seven-point scale with four items including blinding, dropout, randomization and "concealment of treatment allocations" (Hovaguimian et al., 2013). RRs were calculated with 95% CIs for dichotomous data, mean differences with 95% CIs were calculated for continuous data, and all analyses were done using Microsoft Excel 12.2.3, STATA 11 and RevMan. The authors found that high FIO_2 showed statistically significant benefit compared to normal FIO_2 in prevention of late nausea ($p < 0.05$). Contrarily, there was no effect of statistical significance between high and low FIO_2 on PONV. Also, the high FIO_2 group had less incidence of nausea compared to low FIO_2 and vomiting, though the results were not statistically significant. The authors conclude that the prophylactic antiemetic effect of high FIO_2 is weak and that high FIO_2 reduces PONV in patients without prophylactic antiemetic medication to a limited extent. The authors site several articles of conflicting results regarding the use of high inspired oxygen for PONV prevention. The authors admit that the study was slightly limited as it was only conducted on adults, and no prophylactic antiemetic medications were used causing the baseline risk for PONV were elevated and may have caused the high F_{IO2} to have more an effect than it would have had prophylactic antiemetic medication been used. This review brings to light the need for conclusive data regarding supplemental oxygen for PONV prevention and until more research is done, the results of this study cannot definitively conclude anything nor guide clinical practice nor patient care.

Does Supplemental Oxygen Reduce Postoperative Nausea and Vomiting? A Meta-Analysis of Randomized Controlled Trials

Orhan-Sungur, Kranke, Sessler, and Apfel (2008) conducted a meta-analysis of RCTs with a level of evidence of I to "clarify" the effects of supplemental oxygen on prevention of PONV. Multiple databases were searched including MEDLINE, Cochrane Library, and Science Citation Index with search terms including "supplemental oxygen AND anesthesia," and "[oxygen AND (nausea OR vomiting)]' (Orhan-Sungur et al., 2008). The main outcomes were dichotomous data such as absence of presence of vomiting, nausea, or retching with FIO_2 80% compared to FIO_2 30-40%. Three of the authors each independently read and scored the abstracts and reports possibly meeting the inclusion criteria and assessed the articles for quality in areas such as randomization, blinding, allocation concealment, and description of withdrawals. Data was extracted for type of surgery, interventions, outcomes, risk factors, incidence of PONV in zero to six, six to 12 and zero to 24 hours following surgery and put into a Microsoft Excel document. RRs were calculated with a 95% CI comparing supplemental oxygen to room air, and when the CI did not include the number one, it was considered that there was a statistically significant difference between supplemental oxygen and room air. Five RCTs met the inclusion criteria and were included in the study with a total of 860 patients receiving supplemental 80% oxygen and 867 patients receiving standard 30-40% oxygen. The authors found that the RR for developing overall, early and late PONV within the first 24 hours following surgery in patients receiving 80% FIO_2 compared to patients receiving 30-40% FIO_2 were insignificant. It was also found that the data was similar between abdominal, non-abdominal, and all types of surgeries and any differences were statistically insignificant. Additionally, abdominal surgery patients experienced significantly less vomiting with high concentration of supplemental oxygen ($p < 0.05$), however the data was insignificant with the exclusion of two initial studies. There were two studies that presented results of statistical significance indicating that high concentrations of

supplemental oxygen decrease PONV, however the results from these studies were not included in data analysis. The authors conclude that intraoperative supplemental oxygen at 80% FIO_2 has no effect on PONV no matter the type of surgery and should not be recommended as a prophylactic treatment of PONV. While several studies have asserted the beneficial effects of high inspired oxygen on PONV, those results are not fully represented in this study and therefore all results on this topic must be interpreted with caution and should not yet inform clinical practice without further conclusive research.

Supplemental Intravenous Fluid Therapy

Effects of Intraoperative Liberal Fluid Therapy on Postoperative Nausea and Vomiting in Children – A Randomized Controlled Trial

Ashok, Bala, Bharti, Jain and Samujh (2017) state that not only is PONV unpleasant, emetic episodes can cause serious complications including suture dehiscence, aspiration, dehydration and imbalances of electrolytes. The authors conducted a double blind RCT with a level of evidence of II, in India, to determine the efficacy of liberal intraoperative fluid therapy with crystalloids on PONV in children. A power analysis was conducted and determined a need for 67 participants in both the restricted group receiving 10 mL/kg/hr and in the liberal group receiving 30 mL/kg/hr with an α of 0.05. Convenience sampling was used to recruit 75 patients to each group, however two were lost to follow up in the liberal group, and three were lost in the restricted group yielding a total of 73 and 72 participants with analyzable results in each group respectively. Inclusion criteria including being ASA status I or II, being between the ages of three and seven, and being scheduled for elective penile or lower abdominal surgeries for less than one hour. Exclusion criteria included any renal or cardiovascular diseases, antiemetic use within 24 hours of surgery, having a history of PONV, having a BMI of 30 kg/m^2 or more,

having a history of motion sickness, having a contraindication to caudal block, mental retardation, developmental delays or if the parents of the children could not be contacted over the phone. Each of the 150 children were randomized into the restricted or liberal therapy groups via computer generated randomization. All participants were required to fast for the same amount of time, underwent the same anesthesia and caudal blocks, and received either 10 mL/kg/hr or 30 mL/kg/hr IV crystalloid fluid therapy intraoperatively of lactated ringers (LR) with only the anesthesiologist not being blinded to the intervention. A blinded investigator collected data regarding PONV in the PACU including episodes of retching, nausea, and vomiting with the patient receiving 0.1 mg/kg IV ondansetron upon the first episode and if symptoms still were unresolved after 30 minutes, 0.5 mg/kg IV promethazine was administered. The Face, Leg, Activity, Cry, Consolability (FLACC) scale from zero to 10 was used to assess postoperative pain and 15 mg/kg IV paracetamol was given if the FLACC score was four or greater. Additionally, 24 hours after discharge, the parents were interviewed over the phone to assess satisfaction regarding pain and antiemetic therapy on a scale of zero to 10 with zero being completely unsatisfied and 10 being completely satisfied. Quantitative variables were analyzed for normality, data was that normally distributed was analyzed with *U* tests, proportions were analyzed with *t* tests, and variables relating to time were compared with ANOVA. Statistical significance was set to be $p < 0.05$. The authors found that the number of incidences of PONV were significantly higher for the restricted group than the liberal group ($p = 0.021$). Also, the adjusted OR of PONV for the liberal group was 2.24 times higher than the restricted group ($p = 0.022$). The patients in the restricted group consumed significantly more fluids postoperatively within the first six hours ($p = 0.021$) and the incidence of thirst in the restricted group was significantly higher than that of the liberal group ($p <0.00001$). Finally, parent satisfaction was

significantly higher in the liberal group than restricted group ($p = 0.041$). The authors conclude that PONV, thirst and parent satisfaction were all improved by the intervention of intraoperative administration of 30 mL/kg/hr LR solution compared to 10 mL/kg/hr LR solution. Though the study yielded definitive results, these results may not be generalizable to larger populations to patients undergoing more invasive or surgeries lasting longer than one hour.

Preoperative Fluid Bolus and Reduction of Postoperative Nausea and Vomiting in Patients Undergoing Laparoscopic Gynecologic Surgery

Lambert, Wakim and Lambert (2009) site several studies that identify hypovolemia as one of the contributing factors to PONV incidence and because of this reason the authors conducted this study. This randomized controlled, clinical trial with a level of evidence of II was done to determine what effect a preoperative fluid bolus would have on PONV. This study was conducted in a large general hospital in Tennessee, United States. A power analysis was conducted and determined that in order yield results of statistical significant with $p < 0.05$, there was a need for 22 participants in the control group and 22 participants in the experimental group. Through convenience sampling, data was included for a total of 23 participants who received a fluid bolus in the experimental group and 23 participants who received the routine method of fluid replacement therapy after the removal of data from six participants due to noncompliance with study or anesthesia staff. The authors site inclusion criteria as being at least 18 years old, being ASA status I or II, having self-administered a Fleet's enema, not being pregnant, being scheduled for non-emergency and ambulatory surgeries and having fasted since 12:00 midnight the night prior to surgery. Exclusion criteria included having congestive heart failure, a history of heart disease, DM, epilepsy, heart disease relating to the valves, mental disabilities, being a prisoner, having a history of PONV, or anyone taking antiemetics within 24 hours of surgery.

Participants were randomized into two groups however the method of randomization was not explicitly stated. Both participants and researchers were blinded to the interventions. Participants in the intervention group receiving a fluid bolus received up to 1000 mL of LR solution within an hour and the participants in the control group received the routine amount of LR solution as directed by the anesthesiologist. Both control and intervention groups received two mg IV midazolam preoperatively. All participants received general and routine methods of anesthesia. Upon admission to the PACU, patients were assessed for signs of nausea, vomiting or retching without verbal probing from the nurse who was blinded to the intervention. Data was also collected on the use of rescue antiemetics, baseline blood pressure (BP), BP after induction of supplemental fluids, and use of postoperative opioids. Data was analyzed with SPSS software for correlational, parametric and descriptive statistics with statistical significance set at $p < 0.05$. The authors found that there was a significantly correlation between incidence of nausea and vomiting and a decrease in systolic blood pressure in the group receiving routine fluid replacement therapy ($p = 0.006$). Also, the group receiving the fluid bolus experienced significantly fewer episodes of PONV than the control group ($p = 0.0465$). The authors conclude that preoperative intravenous fluid therapy is an effective way to reduce PONV and should be considered a routine therapy in management of PONV. The authors also note that there was a smaller decrease in systolic blood pressure in the group receiving routine fluid replacement therapy than the group receiving the bolus fluids and that bolus fluid therapy may not be an effective therapy for sustaining blood pressure postoperatively. Because this study included wide ranges of types of surgery, was conducted in a large hospital, was randomized and blinded with clear methods explained, this study is likely generalizable to larger populations and is clinically applicable.

Comparison of Dexamethasone or Intravenous Fluids or Combination of Both on Postoperative Nausea, Vomiting, and Pain in Pediatric Strabismus Surgery

Sayed, Riad and Ali (2016) state that up to 80% of pediatric patients receiving strabismus surgery experience PONV and because of this, they conducted this study. This randomized controlled trial with a level of evidence of II was conducted to compare the efficacy of dexamethasone antiemetic therapy combined with super hydration against either monotherapy for PONV in pediatric patients receiving strabismus surgery. The primary outcome for this study was the proportion of PONV in patients in each of the intervention groups and secondary outcomes included VAS scores, total analgesic medication consumption, the use of rescue antiemetics and adverse effects. This study was conducted in Asyut, Egypt. A power analysis was conducted to determine the number of participants necessary to yield results of statistical significance and determined the need for 38 participants in each group. A total of 40 patients were enrolled in each group to allow for possible drop out. Through convenience sampling, a total of 40 participants were included in each group of dexamethasone monotherapy, super hydration monotherapy, and combined dexamethasone with super hydration. The authors site inclusion criteria as having parental consent, being between the ages of six and 12 years of age, undergoing strabismus surgery, being of ASA status I or II, and undergoing general anesthesia. Exclusion criteria for this study included having a BMI in the 95th percentile or higher for sex and age, having DM, mental retardation, using psychoactive drugs or antiemetics within 24 hours of surgery or having a history of GERD. A computer generated random numbers which were then assigned to participants placing them in one of the three groups after IV access was established. The patients receiving dexamethasone monotherapy received 0.15 mg IV dexamethasone one minute before anesthesia induction and intraoperatively received 10

mL/kg/hr of LR solution. The patients receiving super hydration monotherapy intraoperatively received 30 mL/kg/hr of LR solution. The combination group received both 0.15 mg IV dexamethasone one minute before anesthesia induction and intraoperative LR solution of 30 mL/kg/hr. All interventions were conducted in a double-blind fashion in which neither participant nor data collector knew the intervention. All participants had the same preoperative diet, same method of surgery performed by one of four physicians, same general method of anesthesia, same tracheal intubation, and received the same monitoring techniques. Directly following the extubation, each incident of retching and successful vomiting was recorded. Nausea was both observed by a blinded and trained nurse, and was self-reported by patient. PONV was assessed on a scale of zero to three with zero being "no nausea or vomiting" and three being "2 or more episodes of vomiting in 30 minutes" (Sayed et al., 2016). Any patient with a PONV score of three was said to have severe nausea and was given a rescue antiemetic of 0.15 mg/kg IV ondansetron. Pain scores were assessed using a zero to ten VAS with zero being "no pain" and ten being "worst possible pain" (Sayed et al., 2016). Upon parental request or when VAS scores were three or higher, 0.15 mg/kg IV paracetamol was administered to control the pain. All data regarding PONV was put into the timeframes of zero to two hours postoperatively, two to six hours postoperatively and six to 24 hours postoperatively. SPSS software was used to analyze the data which was later presented in the form of standard deviations, percentages, range, mean, and more. Variance was analyzed using the post hoc test, nonparametric data was assessed with the Kruskal-Wallis test, comparisons between groups were conducted via *t* tests, and Chi-squared tests were used to compare frequencies and percentages. The authors found that the incidence of PONV was significantly lower for combination therapy group than either monotherapy group ($p < 0.001$) and that the number of patients experiencing no

PONV was significantly higher in the combination therapy group than either monotherapy group ($p < 0.01$). The researchers also found that nausea alone was significantly lower in the combination therapy group than either monotherapy group ($p < 0.03$). Additionally, rescue antiemetic therapy with ondansetron was significantly lower ($p < 0.001$) and dose used was significantly lower ($p < 0.01$) in the combination therapy group than either monotherapy group. In the end, there were no significant differences between either monotherapy group in incidence of PONV, number of participants experiencing no PONV, number of patients requiring rescue antiemetic use, dose of antiemetic used or VAS scores. The authors conclude that the combination of prophylactic 0.15mg/kg dexamethasone with 30 mL/kg/hr LR is more effective than either monotherapy alone at reducing incidence and severity of PONV. Because the researchers adjusted the amount of fluid therapy to correlate with the amount of time spent fasting, the authors admit that there is potential bias in the form of potentially uncontrolled confounding variables, and in the differences in the amount of fluid therapy administered. Additionally, because this study focused specifically on pediatric strabismus surgery, the results may be difficult to generalize to larger populations. Though this study suffered from several limitations, it is still valid and likely relevant to several clinical settings.

Effect of Intravenous Fluid Therapy on Postoperative Vomiting in Children Undergoing Tonsillectomy

Elgueta et al. (2013) assert that inexpensive prophylactic antiemetics used for POV are often not completely effective and can cause side effects and that an alternative equally cost effective preventative intervention could be supplemental fluid therapy. The authors conducted this randomized controlled trial in Santiago, Chile, with a level of evidence of II to determine the efficacy of super-hydration with LR solution for children undergoing tonsillectomies both with

and without adenoidectomies. A power analysis was conducted and determined the need for 42 participants in each group of control and super-hydration to yield results with a power of 80% and α of 0.05. To allow for possible drop out, 50 participants were recruited via convenience sampling and were enrolled in each of the treatment groups. The authors site inclusion criteria for this study as being between the ages of one and 12 years, being of ASA status I or II, those whose parents provided informed consent, and patients who were undergoing tonsillectomies and/or adenoidectomies under general anesthesia. Exclusion criteria for this study included having a BMI in the 95th percentile or greater, having a history of DM or mental retardation, having a known history of GERD, and those who took antiemetic or psychoactive medications within 24 hours of surgery. The 100 participants were randomized into one of two groups via a computer generated random numbers. All participants were required to fast for at least four hours prior to surgery, received the same method of anesthesia, were intubated via tracheal intubation, had their surgeries performed in the same way and were given intraoperative fluids. Only the rate of fluids administration was different from control to super-hydration group with the control receiving 10 mL/kg/hr LR solution and the super-hydration group receiving 30 mL/kg/hr LR solution in a double-blind fashion. The authors site the reason for only assessing vomiting and retching in data collection as the fact that nausea is very difficult to assess in children. Every episode of vomiting or retching following tracheal extubation and patient arrival in the PACU was recorded with the first incidence of retching, vomiting or both signifying the need for 0.15 mg/kg IV ondansetron. If retching and vomiting continued after 20 minutes following the antiemetic administration of ondansetron, 0.015 mg/kg IV droperidol was administered. Pain was assessed with either a VAS of zero to ten with zero being “no pain” and ten being “worst possible pain” or a Children and Infants Postoperative Pain Scale (CHIPPS) of zero to ten

depending on the age and developmental level of the child being assessed (Elgueta et al., 2013). Pain scores were assessed every 15 minutes for the first hour and every 30 minutes for the second hour. Following discharge at the 24-hour postoperative mark, parents were interviewed via telephone to determine if there was any vomiting or retching at home. Normality of data was analyzed with Q-Q plots and the Shapiro-Wilk test. Between group comparisons were analyzed with *t* tests, the Shapiro-Wilk test, or Wilcoxon rank-sum test. Fisher's tests and Chi-squared tests were used to interpret proportions and all data was considered to be statistically significant with $p < 0.05$ considered the cut off for statistical significance. The authors found that participants receiving 10m L/kg/hr of LR were significantly more likely to experience vomiting or retching than the participants who received intraoperative super-hydration with LR solution ($p = 0.0026$). Despite the relative efficacy at preventing POV compared to hydration with 10 mL/kg/hr LR solution, the authors believe that intraoperative super-hydration alone is not a sufficient prophylactic intervention for POV. The authors conclude that intraoperative super-hydration with 30 mL/kg/hr LR solution is an economic alternative prophylactic intervention to pharmacology in decreasing the risk of POV. This study was conducted on a small and specific population, and because of this it may be difficult to generalize to other populations, however, this study is clinically significant in preventing PONV in children.

Supplemental Intravenous Crystalloids for the Prevention of Postoperative Nausea and Vomiting: Quantitative Review

Apfel et al. (2012) published a meta-analysis of all relevant RCTs with a level of evidence of I in *The British Journal of Anesthesia*. A total of seven authors conducted this study to determine if supplemental IV hydration with crystalloids decreases PON, POV, PONV or use of rescue antiemetics as compared to more traditional fluid therapy. The authors conducted

searches on EmBase, the Cochrane Library, PubMed and Web of Science including terms such as “preoperative,” “hydration,” “crystalloid,” “intraoperative,” “PONV,” and “postanesthesia.” (Apfel et al., 2012). Inclusion criteria for this study included being an adult or adolescent patient at least 16 years old undergoing surgical procedures, and IV hydration with crystalloid solutions. Two authors each reviewed the abstracts and full reports that may have met the inclusion criteria. The same two authors extracted data that was dichotomous in nature such as incidence of PON, incidence of POV, incidence of PONV, use of rescue antiemetics and incidence of side effects from medications. A third author would resolve any discrepancies in data collection and when data from tables was unclear, it was extrapolated via graphs. A total of 15 RCTs were included in the review with a total of 1,570 patients with 787 of them receiving supplemental crystalloid fluid therapy and 783 of them receiving conservative fluid therapy. In this study, the conservative regimen consisted of zero to two mL/kg and the supplemental fluid regime consisted of 15-30 mL/kg. A Cochrane scale for risk for risk of bias was used to analyses the 15 RCTs for quality out of which several showed moderate risk for bias. Meta-analyses were conducted on the data collected with Review Manager 5.1 to determine RRs with CIs of 95% and statistical significance set at $p < 0.05$. The authors found that supplemental crystalloids significantly reduced early PON ($p = 0.003$), late PON ($p = 0.004$) and PON overall ($p = 0.02$) compared to the conservative fluid regimen. Additionally, supplemental crystalloids significantly reduced overall POV ($p = 0.004$) compared to the conservative fluid regimen. Supplemental crystalloids significantly reduced late PONV ($p < 0.001$) and overall PONV ($p = 0.003$). The authors also found that supplemental crystalloids reduced the need for rescue antiemetic medication significantly ($p < 0.001$) compared to the conservative fluid regimen. These findings are consistent with other findings regarding supplemental IV in the treatment and prevention of

PONV. The authors conclude that the use of supplemental IV crystalloids reduces PONV, reduces the need for rescue antiemetic medication, and can be used as a prophylactic antiemetic intervention. While the results of this study are doubtlessly clinically significant and are generalizable to larger populations, this review suffered from several limitations. The authors admit that many of the samples included in the review had treatment sizes of 50 or less which may be why some of the results did not reach statistical significance. Additionally, both preoperative and intraoperative fluid therapies were included which may have influenced the results. Finally, there was a very wide range of fluids administered between studies from two to 30 mL/kg/hr and future studies may be needed to further narrow down the results.

Serotonin $5HT_3$ Antagonists

$5HT_3$ Antagonists for Prophylaxis of Postoperative Nausea and Vomiting in Breast Surgery: A Meta-Analysis

Singhal, Kannan and Gota (2012) conducted a systematic review and meta-analysis with a level of evidence I originally published in the *Journal of Postgraduate Medicine.* This review set out to determine the efficacy of $5HT_3$ antagonists compared to non-$5HT_3$ antagonists for prevention of PONV in women undergoing breast surgeries. The databases searched included the Cochrane Central Register of Controlled Trials and PubMed for terms including "PONV," "prevention," "antiemetic," "mastectomy," and "breast surgery" (Singhal et al., 2012). Two of the three researchers conducted the search and analyzed the articles, titles, abstracts and correspondences for compliance with inclusion criteria including being published in English, RCTs, having patients that were undergoing breast surgeries, comparison one or more $5HT_3$ antagonist with other types of antiemetics or placebo, patients who were undergoing general anesthesia, and antiemetic administration prophylactically as opposed to as a treatment.

Exclusion criteria for this review included trials that evaluated anesthesia other than general anesthesia or used interventions for PONV that were non-pharmacologic. All included articles were assessed for quality using the Jadad scale and scored > 3 therefore determining their quality as good. Publication bias was assessed using funnel plots. A total of 19 RCTs were included in the review with a total of 2,053 participants. In the RCTs analyzed, the control consisted of either placebo or active controls and the intervention consisted of $5HT_3$ agonists. Within this study. the primary outcome included incidence of PONV and secondary outcomes included use of rescue antiemetics for PONV, incidence of nausea and incidence of vomiting. Analysis of subgroup data included duration of surgery, duration of anesthesia, and timing of prophylactic antiemetic administration. Two of the reviewers each independently extracted data from the RCTs including demographic data and primary and secondary outcomes. Data was analyzed via RevMan software with ORs with CI of 95%. The authors found that compared to placebo and active controls, $5HT_3$ antagonists were more effective in preventing PONV, and compared to placebo were also more effective at preventing PON, POV and in decreasing the need for rescue antiemetics. On the other hand, compared to active controls, $5HT_3$ antagonists did not significantly reduce the need for rescue antiemetics. Compared to placebo, the incidence of PONV was significantly reduced for ondansetron ($p = 0.0001$), granisetron ($p < 0.00001$) and for other $5HT_3$ antagonists ($p < 0.00001$). The OR of PONV was reduced by 82% for $5HT_3$ antagonists compared to placebo ($p < 0.0001$). Compared to placebos, $5HT_3$ antagonists did not produce significantly more incidences of adverse effects. $5HT_3$ antagonists compared to active controls significantly better prevented PONV (P = 0.01) but did not have a significant effect on need for recue antiemetics. Granisetron either combined with dexamethasone or droperidol was more effective in combating PONV ($p = 0.002$). The authors conclude that $5HT_3$ antagonists are

effective at reducing PON, POV, and reducing the need for rescue antiemetics with granisetron and ondansetron being most effective at preventing POV. Additionally, the authors conclude that $5HT_3$ antagonists should be considered primary prophylactic agents to prevent PONV in women undergoing breast surgery. The authors admit that their findings are not consistent with the findings of a Cochrane review regarding specific drugs and their efficacy, however both studies indicate that $5HT_3$ antagonists are effective for PONV prevention and treatment. The authors admit that all but one study used the recommended optimal dose of 4mg ondansetron which may have influenced results very slightly. Despite this small limitation, this study produced high quality evidence that is generalizable to larger populations and is clinically relevant for improving patient care and patient outcomes.

Comparative Safety of Serotonin ($5HT_3$) Receptor Antagonists in Patients Undergoing Surgery: A Systematic Review and Meta-Analysis

Tricco et al. (2015) produced a systematic review and meta-analysis with a level of evidence of I under BMC Medicine to determine the safeties of different $5HT_3$ antagonists. A total of 21 authors produced the review. An experienced librarian searched for articles in MEDLINE, the Cochrane Central Register of Controlled Trials and EmBase though the authors to not explicitly state which terms were searched for within these databases. Eligibility criteria for this review including being a CCT, RCT, quasi-experimental RCT, quasi-experimental study, or cohort study originally published in English involving patients who received $5HT_3$ antagonists for PON, POV, or PONV and underwent surgery of any kind. The primary outcome being explored was the incidence of arrhythmias with secondary outcomes being mortality, delirium, PR elongation and QT elongation. Pairs of reviewers independently screened potential articles for compliance with inclusion criteria, to abstract data, and to analyze the quality of evidence of

the selected articles with discrepancies being resolved via discussions. A total of 120 studies of various designs were included in analysis with a total of 27,787 participants with 97% of the studies being RCTs. To assess for quality and bias, quasi-experimental studies were assessed using the "Cochrane Effective Practice and Organization of Care risk for bias tool," and cohort studies were assessed using the "Newcastle-Ottawa Scale," and all studies that reported harm were assessed using the "McMaster Quality Assessment Scale of Harms" (Tricco et al., 2015). The authors found that compared to patients receiving placebo, dolasetron, granisetron, ondansetron and ondansetron combined with dexamethasone, the patients receiving granisetron combined with dexamethasone experienced significantly higher numbers of arrhythmias. Additionally, in terms of arrhythmias, dolasetron and ondansetron in combination with dexamethasone are safest overall, and ondansetron in combination with dexamethasone is safest for children if administered intraoperatively. No significant differences in delirium or mortality existed between different $5HT_3$ antagonists. The authors conclude that granisetron plus dexamethasone may increase the risk for cardiac arrhythmias. The authors do not state if the results are consistent with other studies potentially because this was one of the first studies in this area, however they do state that the results "were consistent across subgroup and sensitivity analysis" (Tricco et al., 2015). The authors also admit there were several limitations to their review including the fact that follow up time period varied greatly from under six hours to greater than a week. Additionally, one of the authors owns stock in a company that produces medication used in one intervention. Even more, not all results in this study were RCT, and the quasi-experimental studies often had high risk for bias. Despite these limitations, the rigor of this study is good, and the study is very important clinically. The results can and should be applied to

larger populations to improve patient outcomes and prevent the adverse effects of arrhythmias in patients receiving granisetron with dexamethasone.

Comparison of the Efficacy of Ondansetron and Granisetron to Prevent Postoperative Nausea and Vomiting After Laparoscopic Cholecystectomy: A Systematic Review and Meta-Analysis

Wu et al. (2013) conducted a systematic review and meta-analysis of RCTs with a level of evidence of I in *Surgical Laparoscopy, Endoscopy & Percutaneous Techniques* order to determine the efficacy of ondansetron and granisetron on PONV in patients undergoing laparoscopic cholecystectomies. A total of four authors conducted the review. Databases searched included MEDLINE, the Science Citation Index Expanded, Cochrane Register of Controlled Trials, EmBase, PubMed, Google Scholar, Chinese Biomedical Database, and China National Knowledge Infrastructure Whole Article Database. Search terms included "laparoscopic cholecystectomy," "Zofran," "ondansetron," and "granisetron" (Wu et al., 2013). The primary author reviewed article titles and abstracts to exclude articles based on relevance to the review, two authors reviewed titles, abstracts, and keywords for relevance and then obtained the full texts of the articles with discrepancies being resolved via discussion. Inclusion criteria for this review included RCTs, patients who underwent laparoscopic cholecystectomies exclusively, received interventions of prophylactic IV ondansetron and/or prophylactic IV granisetron in comparison with each other and measured the incidence of early PONV and total PONV. Two of the four authors assessed all studies for methodological quality for areas including blinding, randomization, selective reporting, sources of funding, differences in baselines, study design and allocation concealment. A total of five RCTs with a total of 244 participants were included in the systematic review and meta-analysis. The authors found that the incidence is PONV in the early

postoperative period were higher for those receiving ondansetron than those receiving granisetron though the differences were not statistically significant. Additionally, PONV total incidence was higher for those receiving ondansetron than those receiving granisetron though the differences were not statistically significant. The need for rescue antiemetics was higher for those receiving ondansetron than those receiving granisetron though the differences were not statistically significant. Finally, the number of patients with headaches was fewer in the ondansetron groups than the granisetron groups though the difference was not statistically significant. The authors conclude that ondansetron and granisetron are equally effective at preventing PONV. Despite these results, the review suffered from several limitations. Two of the five studies presented unclear risk for bias while 3 presented high risk for bias. The authors also mention that there may be a relationship between dose and effect of medication; one study adopted doses that may have caused it to appear that ondansetron has better therapeutic effects. The authors mention that there is further need for research on dose and effect of both ondansetron and granisetron. Due to the evidence of publication bias within this review and for the results mentioned above, the results should be interpreted with caution.

Dexamethasone, Ondansetron, and their Combination and Postoperative Nausea and Vomiting in Children Undergoing Strabismus Surgery: A Meta-Analysis of Randomized Controlled Trials

Shen et al. (2014) published a systematic review and meta-analysis of RCTs with a level of evidence of I in *Pediatric Anesthesia* to determine the safety and efficacy of ondansetron and dexamethasone on PONV in pediatric patients receiving surgery for strabismus. A total of five authors published the review. The primary outcome being explored was incidence of PONV within 24 hours of surgery and secondary outcomes included the need for rescue antiemetics and

complications. Databases searched included MEDLINE, PubMed, EmBase, Cochrane databases and SCOPUS for terms including “strabismus,” “postoperative,” “PONV,” “nausea,” “vomiting,” “dexamethasone,” “glucocorticoid,” “steroid,” “antiserotonin,” and “ondansetron” in articles published up to November of 2013 (Shen et al., 2014). Inclusion criteria for studies included being a RCT comparing ondansetron or dexamethasone and placebo in pediatric strabismus surgery patients, clearly listing all protocols and drugs used and clearly defining vomiting and nausea. Exclusion criteria for this review included studies in which participants were receiving surgeries other than strabismus surgeries, if ondansetron or dexamethasone were administered via any route other than intravenously, if outcomes were not clearly reported, or if there was any overlap between cohorts, authors or centers in which the interventions were conducted. A total of 13 RCTs were selected for analysis with a total of 2,006 patients with the control being treated as an active control or placebo and the intervention consisting of $5HT_3$ antagonists. Two of the five authors independently extracted data and a third author resolved any discrepancies regarding the data collection between the other two authors. Two of the five authors reviewed each article and assessed them for quality in regard to allocation concealment, blinding, randomization, dropouts and other biases with a third author resolving any discrepancies in these analyses. All articles were found to be of good methodological quality and had strong evidence. Statistical analysis was conducted according to the Cochrane Collaboration recommendations as well as the guidelines of Quality of Reporting of Meta-Analyses PRISMA. The authors found that compared to placebo, incidences of POV with prophylactic dexamethasone were significantly reduced ($p = 0.0002$). Doses of dexamethasone compared to placebo 0.25mg/kg, 0.5 mg/kg and 1 mg/kg in relation to incidence of POV were not significantly different. Also, compared to placebo, incidences of PONV with prophylactic

ondansetron were significantly lower ($p < 0.0005$) and significantly reduced the need for rescue antiemetics ($p < 0.00001$). Dexamethasone combined with ondansetron compared to ondansetron alone significantly reduced incidence of POV ($p = 0.0002$). The authors conclude that the overall incidence of PONV in comparison between dexamethasone and ondansetron was not significantly different nor was the need for rescue antiemetic medication. Finally, prophylactic ondansetron or dexamethasone improves PONV in pediatric strabismus surgery. Ondansetron reduces the need for rescue antiemetic medication, and a combination of ondansetron and dexamethasone should be administered prophylactically to reduce overall PONV. Shen et al. (2014) state that their review is consistent with others. Due to the strong quality of evidence, these results are clinically applicable though they may not be generalizable to larger populations.

Dexamethasone Combined with Other Antiemetics Versus Single Antiemetics for Prevention of Postoperative Nausea and Vomiting after Laparoscopic Cholecystectomy: An Updated Systematic Review and Meta-Analysis

Awad et al., (2016) updated a systematic review and meta-analysis with a level of evidence of I in the *International Journal of Surgery* in order to determine both the safety and efficacy of dexamethasone combined with other antiemetics compared to monotherapy antiemetics in preventing PONV in laparoscopic cholecystectomy patients. A total of seven authors published the review. The authors searched for articles published up to August of 2016 in databases including SCOPUS, PubMed, EmBase, and Web of Science using the keywords of "dexamethasone AND cholecystectomy" (Awad et al., 2016). Four authors screened the titles and abstracts for relevance and then screened the full text for compliance with inclusion and exclusion criteria. Inclusion criteria for this review included being a RCT, comparing single antiemetics with dexamethasone in combination with another antiemetic, reporting of incidence

of PONV as dichotomous and involving patients who received laparoscopic cholecystectomies. Exclusion criteria for this review included studies that were observational, non-randomized, reviews, theses, were chapters of books, studies that were not available in full text format, studies that were not available in English, studies that had unreliable data, and studies that had been retracted due to false data. A total of 14 RCTs were included in this review with a total of 1542 participants; 816 participants in the combination antiemetic groups and 726 patients in the single antiemetic groups. Two of the seven authors extracted data independently. Data was classified into three periods of PONV including early PONV of zero to two hours, zero to four hours or zero to six hours, late PONV of more than six hours and overall PONV of zero to 24 hours. Two of the seven authors analyzed all articles for quality using "The Cochrane Collaboration risk of bias tool" and found that all articles were of moderate to high quality (Awad et al., 2016). The authors found that dexamethasone in combination with additional antiemetics compared to single antiemetics was significantly more beneficial for reducing early PONV ($p < 0.0001$), late PONV ($p < 0.0001$) and overall PONV ($p < 0.0001$) and also decreased need for a rescue antiemetic ($p < 0.0001$). Single antiemetic and combination of dexamethasone and additional antiemetic medication did not show significant differences in incidence of adverse effects including sedation, urinary retention, headache, itching or dizziness suggesting that combination with dexamethasone is no more dangerous than single antiemetic medication for PONV prevention. Dexamethasone in combination with ondansetron compared to ondansetron alone was significantly more beneficial for reducing early PONV ($p = 0.005$), late PONV ($p = 0.008$) and overall PONV ($p = 0.02$) as well as decreased need for a rescue antiemetic ($p = 0.03$). Dexamethasone with metoclopramide compared to metoclopramide alone was significantly more beneficial for reducing early PONV ($p = 0.0004$), late PONV ($p = 0.0002$) and overall PONV (p

< 0.0001). Dexamethasone in combination with ramosetron compared to ramosetron alone was not statistically more beneficial for reducing early, late or overall PONV but significantly decreased need for a rescue antiemetic ($p = 0.01$). Dexamethasone in combination with dolasetron compared to dolasetron alone was significantly more beneficial for reducing overall PONV ($p < 0.0002$). Dexamethasone in combination with ondansetron compared to dexamethasone alone was significantly more beneficial for reducing overall PONV ($p = 0.02$) as well as decreased need for a rescue antiemetic ($p = 0.03$). Dexamethasone combined with granisetron compared to granisetron alone was significantly more beneficial for reducing overall PONV ($p = 0.03$). Dexamethasone combined with palonosetron compared to palonosetron alone was significantly more beneficial for reducing early PONV ($p = 0.002$) and overall PONV ($p < 0.0001$) as well as decreased need for a rescue antiemetic ($p = 0.005$). The authors conclude that dexamethasone in combination with other antiemetics is more beneficial for preventing PONV and reduces the need for other rescue antiemetics except for combination of dexamethasone with ramosetron which was not as beneficial in any postoperative period and dexamethasone with granisetron which was not as beneficial in the early postoperative period. One limitation of this was that for the studies that did not report data on overall PONV from zero to 24 hours, the researchers used data from the highest number of incidences in the longest timeframe specified in the study which may have influenced the results regarding the overall PONV period. Similarly, depending on the study, early PONV was defined as zero to two hours, zero to four hours or zero to six hours and PONV could be different in the first two hours than the first six which may have also affected the results regarding early PONV. The data provided on dolasetron, granisetron and palonosetron came from single studies and therefore more research is needed to definitively comment on their effect when combined with dexamethasone compared to

their single use in prevention of PONV. Despite these limitations, this study is of a high level of evidence including only studies of moderate to high quality and yielded strong results. For these reasons. the study is clinically applicable and should be used to better patients' outcomes and care.

Conclusion

The articles reviewed in this chapter addressed several of the integrative therapies available to prevent and treat PONV including aromatherapy, P6 acupuncture, supplemental oxygen, supplemental IV fluid therapy and $5HT_3$ pharmacotherapy. The 27 articles reviewed included quasi-experimental studies, RCTs, systematic reviews and meta-analyses ranging from a level of evidence of I to III. The literature revealed that PONV is a complex issue with many facets and that not one approach of managing PONV is perfect. The cost-benefit analysis for treatments and interventions in healthcare are often very important. The literature reviewed provided sound evidence for cost-effective treatments such as deep breathing (N = 2), aromatherapy with IPA, ginger or peppermint oil (N = 5), P6 wrist acupuncture (N = 5) and supplemental IV fluid therapy (N = 4). Overall, the results of the literature reviewed indicate a variety of effective treatment options for patients experiencing PONV ranging from minimally invasive all the way to pharmacotherapy. The variety of effective interventions allow for both healthcare professionals and patients the freedom of choice in treatment. Additionally, the variety of treatment options allow for nursing staff to utilize the principles of integrative nursing starting with the least invasive and intensive treatment possible and working their way up.

Future research exploring which scents of essential oils are beneficial in aromatherapy to manage PONV would be very beneficial. The results yielded from the studies regarding aromatherapy were varied, likely due to the personal preferences and sensitivities to scent.

Additionally, it is unclear as to whether the beneficial effects of aromatherapy are from the inhalant or from the nature of deep breathing itself that accompanied the majority of aromatherapy interventions explored in this thesis (Cronin et al., 2015). Furthermore, additional research exploring intraoperative fluid therapy versus preoperative fluid therapy would better guide clinicians in their use of supplemental IV fluid therapy to prevent PONV. Based on this review of literature, the evidence-based best practice recommendations in place for treating and managing PONV need to be updated to include more of the alternative therapies to allow for better patient care and additional opportunities for nursing staff to successfully employ the principles of integrative nursing.

CHAPTER 3

Best Practice Recommendations: Prevention and Treatment of PONV

The purpose of this thesis was to create best practice recommendations to both treat and prevent PONV with an integrative nursing approach moving from interventions of least invasive to most in order to reduce the post-surgical complications, healthcare costs and labor associated with increased PONV. The proposed best practice recommendations in Table 1 will help nursing and healthcare staff to reduce the episodes of PONV and better tailor their approaches to treating and managing PONV to each patient.

The literature reviewed in Chapter 2 provided valuable information on some of the most common interventions used in the PACU for management of PONV as well as some both promising and emerging interventions used for PONV. As the considerable amounts of research show, the nursing interventions used to manage PONV do not fully alleviate the unpleasant and potentially dangerous condition that 20% to 30% of all postoperative patients face (Cutshall & Van Getson, 2014). Because PONV is a multifaceted healthcare issue, it requires a multifaceted approach to management as well. The review of literature details the beneficial effect of using acupuncture on the P6 acupoint site, liberal supplemental fluid therapy with crystalloid solutions and the use of ondansetron in combination with dexamethasone for treating and preventing PONV. While the effects of aromatherapy and supplemental oxygen on PONV are also explored in this thesis, the results have a weak beneficial effect and are not considered strong evidence. Because the research on aromatherapy and supplemental oxygen is weak, the best practice recommendations for both modalities must be interpreted with caution and if used, used sparingly and appropriately.

The levels of evidence in the following tables is derived from a rating system for the hierarchy of evidence (Guayatt & Rennie, 2002). Based on this rating system, level I evidence includes meta-analysis or systematic reviews of all RCTs that may be relevant. Level II evidence includes RCTs that are of rigorous design. Level of evidence of III includes controlled trials that lack randomization but are well-designed. Data that was from case-control, cohort, qualitative, or descriptive studies were determined of a level of evidence greater than III and therefore not strong evidence and were not further analyzed in this honors thesis (Guayatt & Rennie, 2002).

Table 1

Best Practice Recommendation for Use of Aromatherapy for Prevention and Treatment of PONV

Recommendation	Rationale	References	Level of Evidence
Use of Inhaled Ginger Essential Oil	Ginger has powerful antiemetic properties, can reduce gastrointestinal distress and is an effective antiemetic that can be used for PONV including patients undergoing abdominal surgeries.	Adib-Hajbaghery, M., Hosseini, F. S. (2015). Investigating the effects of inhaling ginger essence of post-nephrectomy nausea and vomiting. *Complementary Therapies in Medicine, 23*(6), 827-831. doi: 10.1016/j.ctim.2015.10.002	Level II
		Lee, Y. R., & Shin, H. S. (2017). Effectiveness of ginger essential oil on postoperative nausea and vomiting in abdominal surgery patients. *The Journal of Alternative and Complementary Medicine, 23*(3), 196-200. doi: 10.1089/acm.2015.0328	Level III
Use of Inhaled Peppermint Oil	Peppermint oil can reduce intensity of nausea and increases in effectivity for controlled PONV when used in conjunction with controlled breathing.	Briggs, P., Hawrylack, H., & Mooney, R. (2016). Inhaled peppermint oil for postop nausea in patients undergoing cardiac surgery. *Nursing2016, 46*(7), 61-67. doi: 10.1097/01.NURSE.0000482882.38607.5c	Level III
		Sites, D. S., Johnson, N. T., Miller, J. A., Torbush, P. H., Hardin, J. S., Knowles, S. S., … Tart, R. C. (2014). Controlled breathing with or without peppermint aromatherapy for postoperative nausea and/or vomiting symptom relief: a randomized controlled trial. *Journal of PeriAnesthesia Nursing, 29*(1), 12-19. doi: 10.1016/j.jopan.2013.09.008	Level II

Implementation of Controlled Breathing Exercises	Controlled breathing both with and without inhaled aromatherapies of peppermint oil and isopropyl alcohol may decrease PONV.	Cronin, S. N., Odom-Forren, J., Roberts, H., Thomas, M., Williams, S., & Wright, M. I. (2015). Effects of controlled breathing, with or without aromatherapy, in the treatment of postoperative nausea. *Journal of PeriAnesthesia Nursing, 30*(5), 389-397. doi: 10.1016/j.jopan.2015.03.010	Level III
		Sites, D. S., Johnson, N. T., Miller, J. A., Torbush, P. H., Hardin, J. S., Knowles, S. S., … Tart, R. C. (2014). Controlled breathing with or without peppermint aromatherapy for postoperative nausea and/or vomiting symptom relief: a randomized controlled trial. *Journal of PeriAnesthesia Nursing, 29*(1), 12-19. doi: 10.1016/j.jopan.2013.09.008	Level II
Use of Inhaled Isopropyl Alcohol	Inhaled isopropyl alcohol is as effective as promethazine for treatment of PONV, is more cost effective, is easier to administer and works faster.	Pellegrini, J., DeLoge, J,. Bennet, J., & Kelly, J. (2009). Comparison of inhalation of isopropyl alcohol vs promethazine in treatment of postoperative nausea and vomiting (PONV) in patients identified as at high risk for developing PONV. *AANA Journal*, 77(4), 293-299.	Level II

While there are potential positive benefits of inhaled essential oils and controlled breathing with ginger essential oil, peppermint oil and isopropyl alcohol, these results should be interpreted with caution and the benefit of intervention may in fact come from deep breathing. Hines et al. (2018) assert in a systematic review with level of evidence of I that the data regarding aromatherapy as treatment for PONV is of low quality and may reduce use of rescue antiemetics and have effectivities similar to those of placebos and much more research is needed to determine the true efficacy of inhaled aromatherapy for treatment of PONV.

Table 2

Best Practice Recommendation Using P6 Acupoint Acupuncture for Prevention and Treatment of PONV

Recommendation	Rationale	References	Level of Evidence
Implementation of Intraoperative P6 Acupoint Acupuncture	Intraoperative P6 acupuncture is effective at reducing PONV for both adult and pediatric patients. Intraoperative P6 acupuncture may be as effective or more effective at reducing PONV than metoclopramide, metoclopramide with dexamethasone and other traditional pharmacotherapies. Additionally, intraoperative P6 acupuncture has less side effects and is more cost effective than traditional pharmacotherapy used to manage PONV.	Albooghobeish, M., Mohtadi, A., Saidkhani, V., Fallah, H., Behaein, K., Nesionpour, S., & Nikbakht, R. (2017). Comparison between effects of acupuncture and metoclopramide on postoperative nausea and vomiting after gynaecological laparoscopy: a randomized controlled trial. *Anesthesiology and Pain Medicine, 7*(5). doi: 10.5812/aapm.12876	Level II
		Bakhshaei, M. H., Khoshraftar, E., Shoja, S., & Mehrabi S. (2018). Comparison of wrist acupuncture point P6 with pharmacologic management to prevent postoperative nausea and vomiting in patients undergoing laparotomy: a double blind study. *World Family Medicine, 16*(2), 73-76. doi: 10.5742/MEWFM.2018.93242	Level II
		Shin, H. C., Kim, J. S., Lee, S. K., Kwon, S. H., Kim, M. S., Lee, E. J., & Yoon, Y. J. (2016). The effect of acupuncture on postoperative nausea and vomiting after pediatric tonsillectomy: A meta-analysis and systematic review. *The Laryngoscope*, *126*(8), 1761-1767. doi: http://dx.doi.org.ezproxy4.library.arizona.edu/10.1002/lary.25883	Level I

Implementation of P6 Acupoint Acupuncture	Acupuncture of acupoint P6 greatly reduces the need for rescue antiemetics, incidences of PONV and is as effective as traditional antiemetic pharmacotherapies for treating PONV.	Lee, A., Chan, S., & Fan, L. (2015). Stimulation of the wrist acupuncture point PC6 for preventing postoperative nausea and vomiting (review). *Cochrane Database of Systematic Reviews, 11.* doi: 10.1002/14651858.CD003281.pub4	Level I
Implementation of Acupuncture of Acupoint P6 in Conjunction with Other Acupoints	The effectivity of acupuncture at acupoint P6 for reducing incidence of PONV increases significantly when combined with additional acupoints.	Cheong, K. B., Zhang, J., Huang, Y., & Zhang, Z. (2013). The effectiveness of acupuncture in prevention and treatment of postoperative nausea and vomiting – a systematic review and meta-analysis. *PLoS One, 8*(12). doi: 10.137/journal.pone.0082474	Level I

All research reviewed regarding acupuncture using the P6 acupoint site overwhelmingly indicate that it is effective at managing PONV when used intraoperatively, postoperatively, unilaterally, bilaterally, in conjunction with pharmacologic antiemetics and when used alone. Lee et al. (2015) assert that stimulation of the P6 acupoint both through acupressure and acupuncture is comparable to antiemetics. Though this thesis does not focus on the benefits of acupressure of the P6 acupoint, it is beneficial and can be used in conjunction with acupuncture of the P6 acupoint as demonstrated by Lee et al. (2015). Additionally, as demonstrated in the systematic review and meta-analysis conducted by Cheong et al. (2013), acupuncture of P6 acupoints in conjunction with other acupoints is beneficial for PONV as well. Additional research needs to be done to identify the optimal duration, timing, depths and combinations of acupoints.

Table 3

Best Practice Recommendation Using Supplemental Inspired Oxygen for Prevention and Treatment of PONV

Recommendation	Rationale	References	Level of Evidence
Provision of high intraoperative inspired oxygen (80%) for those at high risk of developing PONV	High inspired oxygen of 80% may reduce episodes of early POV and late PON although it does not reduce PONV.	Šimurina, T., Mraović, B., Mikulandra, S., Sonicki, Z., Sulen, N., Dukić, B., & Gan, T. J. (2010). Effects of high intraoperative inspired oxygen on postoperative nausea and vomiting in gynecologic laparoscopic surgery. *Journal of Clinical Anesthesia, 22*(7), 492-498. doi: 10.1016/j.jclinane.2009.10.013	Level II
		Hovaguimian, F., Lysakowski, C., Elia, N., & Tramèr, M. R. (2013). Effect of intraoperative high inspired oxygen fraction on surgical site infection, postoperative nausea and vomiting, and pulmonary function: systematic review and meta-analysis of randomized controlled trials. *Anesthesiology, 119*(2), 303-316.	Level I

While research regarding the use of high-flow inspired oxygen for PONV has been conflicting in the past, the research reviewed in this article found that it has at best a weak effect on improving PONV. In a RCT, Šimurina et al. (2010) found that high inspired 80% oxygen can reduce early POV, overall it had very little effect on PONV. Additionally, Hovaguimian et al. (2013) found that 80% oxygen had a beneficial effect on late PON alone and not on PONV. The remainder of the articles reviewed in this thesis indicate no positive benefit of using high inspired for prevention or treatment of PONV regardless of the type of surgery.

Table 4

Best Practice Recommendation Using Supplemental Intravenous Hydration for Prevention and Treatment of PONV

Recommendation	Rationale	References	Level of Evidence
Provision of liberal intraoperative supplemental crystalloid intravenous hydration of 30 mL/kg/hr	Liberal intraoperative supplemental intravenous hydration with lactated Ringer's solutions reduces incidence of PONV, reduces use of rescue antiemetics and reduces the thirst and fluids consumed postoperatively.	Ashok, V., Bala, I,. Bharti, N., Jain, D., & Samujh, R. (2017). Effects of intraoperative liberal fluid therapy on postoperative nausea and vomiting in children – a randomized controlled trial. *Pediatric Anesthesia, 27*, 810-815. doi: 10.1111/pan.13179	Level II
		Elgueta, M. F., Echevarría, G. C., De la Fuente, N., Cabrera, F., Valderrama, A., Cabezón, R… & Cortinez, L. I. (2013). Effect of intravenous fluid therapy on postoperative vomiting in children undergoing tonsillectomy. *British Journal of Anesthesia, 110*(4), 607-614. doi:10.1093/bja/aes453	Level II
		Apfel, C. C., Meyer, A., Orhan-Sungur, M., Jalota, L., Whelan, R. P., & Jukar-Rao, S. (2012). Supplemental intravenous crystalloids for the prevention of postoperative nausea and vomiting: quantitative review. *British Journal of Anesthesia, 108*(6), 893-902. doi: 10.1093/bja/aes138	Level I

Provision of a combination of liberal intraoperative supplemental crystalloid intravenous hydration of 30 mL/kg/hr in conjunction with preoperative 0.15 mg/kg dexamethasone	Combined liberal fluid therapy with dexamethasone is more effective than either monotherapy in reducing both the incidence and severity of PONV, reducing the need for rescue antiemetics.	Sayed, J. A., Riad, M. A., & Ali, M. O. (2016). Comparison of dexamethasone or intravenous fluids or combination of both on postoperative nausea, vomiting and pain in pediatric strabismus surgery. *Journal of Clinical Anesthesia, 34*, 136-142. doi: 10.1016/j.jclinane.2016.03.049	Level II

Lambert el al. (2009) site dehydration and hypovolemia as some of the common contributing factors of developing PONV and it is no wonder that many of the interventions described to correct fluid loss or increase fluids also decreased PONV. Interestingly, Ashok et al. (2017) found that those who received liberal amounts of fluid 30 mL/kg/hr compared to the standard fluids of 10 mL/kg/hr not only lower levels of PONV but also lower levels of thirst. A known risk factor for PONV is “premature oral intake” (Cuthshall & Van Getson, 2014, p. 217), and therefore the decreased thirst of patients following intraoperative liberal fluid therapy may be of benefit in preventing PONV. An RCT conducted by Lambert et al. (2009) also found there to be beneficial effects of a fluid bolus of lactated Ringer’s solution of up to 1,000 mL by decreasing episodes of PONV and to have a beneficial effect on systolic blood pressures when compared to the traditional methods of fluid therapy. While this is a high quality study with high quality evidence, it was conducted almost 10 years ago and the surplus of recent research indicating the use of 30 mL/kg/hr of lactated Ringer’s solution seems a more credible intervention to suggest.

Table 5

Best Practice Recommendation Pharmacotherapies for Prevention and Treatment of PONV

Recommendation	Rationale	References	Level of Evidence
Use of ondansetron as first line prophylactic pharmacotherapy for PONV	$5HT_3$ antagonists reduce are more effective at preventing PONV than active controls, do not cause additional adverse effects and reduce the need for rescue antiemetics. Additionally, of the $5HT_3$ antagonists combined with dexamethasone, ondansetron and dolasetron were found to be safest for cardiac events with ondansetron being safest for children.	Singhal, A. K., Kannan, S. & Gota, V. S. (2012). $5HT_3$ antagonists for prophylaxis of postoperative nausea and vomiting in breast surgery: A meta-analysis. *Journal of Postgraduate Medicine, 58*(1), 23-31.	Level I
		Tricco, A. C., Soobiah, C., Blondal, E., Veroniki, A. A., Khan, P. A., Vafaei, A.,…Straus, S. E. (2015). Comparative safety of serotonin (5-HT_3) receptor antagonists in patients undergoing surgery: a systematic review and meta-analysis. *BMC Medicine, 13*(1), 142. doi: 10.1186/s12916-015-0379-3.	Level I
Combination of prophylactic dexamethasone and ondansetron	Ondansetron when combined with dexamethasone reduces PONV more than either monotherapy, reduces the need for additional rescue antiemetics and does not produce additional adverse effects from combination therapies.	Shen, Y. D., Chen, C. Y., Wu, C. H., Cherng, Y. G., & Tam, K. W. (2014). Dexamethasone, ondansetron, and their combination and postoperative nausea and vomiting in children undergoing strabismus surgery: a meta-analysis of randomized controlled trials. *Pediatric Anesthesia, 24*, 490-498. doi: 10.1111/pan.12374	Level I

	Awad, K., Ahmed, H., Abushouk, A. I., Nahrawi, S. A., Elsherbeny, M. Y., Mustafa, S. M., & Attia, A. (2016). Dexamethasone combined with other antiemetics versus single antiemetics for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: an updated systematic review and meta-analysis. *International Journal of Surgery, 36,* 152-163. doi: 10.1016/j.ijsu.2016.10.034	Level I

Where Singhal et al. (2012) found $5HT_3$ receptor antagonists to be the more effective than the active controls of pharmacologic agents commonly used to prevent PONV, they also found ondansetron to be safest for both children and adults when combined with dexamethasone. Tricco et al. (2015) found that when combined with dexamethasone, the $5HT_3$ antagonists improve in efficacy significantly. Additionally, it was found that granisetron when combined with dexamethasone may increase the risk for cardiac arrhythmias (Tricco et al., 2015). Wu et al. (2013) found that ondansetron and granisetron were equally effective at preventing PONV and that there were no significant differences in incidence of PONV, the need for rescue antiemetics or headaches. Because of the safety concerns of granisetron and the overall effectivity of ondansetron when compared to the other $5HT_3$ antagonists and when combined with dexamethasone, ondansetron should the recommended pharmacotherapy to prevent PONV with a combination of dexamethasone pharmacotherapy.

CHAPTER 4

Implementation to Nursing Practice and Evaluation

Chapter 4 will be centered around implementing integrative therapies to prevent and treat PONV occurring in the first 24 postoperative hours into existing nursing practice. The proposed implementation will include a proposed best practice guideline to be used preoperatively, intraoperatively and postoperatively by healthcare providers for integrative management of PONV. This best practice guideline will be translated into standing orders for all surgical and postoperative patients and integrated into facility policies and procedures. While the ultimate goal is to better prevent and treat PONV, it is crucial to understand if the best practice guideline is beneficial in the clinical setting and how it may be better improved. The desire for continued improvement of the best practice guideline suggests the need for a method of implementation and evaluation that continually assess the efficacy of the guideline once applied. For these reasons, both the implementation and evaluation of this best practice guideline will be based on the Plan-Do-Study-Act (PDSA) cycle. The PDSA cycle is a tool commonly used to implement and to evaluate continuous improvements by healthcare organizations and facilities regarding evidence based research (Institute for Healthcare Improvement, 2017). In order to test the efficacy of the proposed best practice guideline in the clinical setting, it is prudent to first integrate the guideline into small settings, adjust and improve the guideline before expanding the application. For this reason, the proposed guideline will be carried out in a single hospital and evaluated on a biannual basis using the PDSA cycle. Implementation of this best practice guideline will be explored through the “plan” and “do” sections of the cycle while evaluation of the implementation will be explored through the “study” and “act” sections of the cycle (Institute

for Healthcare Improvement, 2017). The final portions of this chapter will include the strengths and limitations of this honors thesis as well as a discussion on areas of future research.

Implementation

Plan

The first part of the PDSA cycle is the planning which includes refining the objective, predictions, and all of the specifics surrounding the specific action (Institute for Healthcare Improvement, 2017). The plan section of the PDSA cycle is what will guide the implementation of the best practice guideline for treating and preventing PONV into the clinical setting. The objective for implementing this best practice guideline into the clinical setting is to reduce the episodes and severity of PONV for patients within the first 24 hours who underwent surgery under general anesthesia. Through implementation of the best practice guideline, it can be hypothesized that both episodes and severity of PONV will be reduced in the first 24 hours following surgery under general anesthesia.

The specific interventions found to be beneficial, as described in Chapter 3, will be integrated into a standardized clinical protocol or intervention bundle and standing surgical and postoperative orders at a single hospital. The bundle includes pre-operative, intraoperative, and post-operative interventions as outlined below. Please see the corresponding table outlining implementations regarding timing below. As part of the bundle, prior to surgery, each patient will be educated on controlled breathing exercises by their nurse and asked to complete a questionnaire regarding their personal risk factors for developing PONV. Additionally, each patient will be provided information about acupuncture and the reduction of PONV associated with it. Each patient will then be given the option to sign a consent for intraoperative acupuncture for the purposes of reducing PONV. For all patients, an infusion of lactated

Ringer's solution with a rate of 30 mL/kg/hr will be given intraoperatively. All patients will receive standard doses of ondansetron in combination with dexamethasone as prophylactic treatment for PONV during the peri-operative period according to facility standards. For patients with multiple risk factors for developing PONV, 0.15 mg/kg dexamethasone will be given prior to induction of anesthesia. All patients will receive acupuncture stimulation of acupoint P6 intraoperatively. At the first report of nausea or vomiting, the postoperative nurse will guide the patient through the controlled breathing exercises taught in the preoperative setting.

Table 6

Timing of Interventions of Care Bundle

Preoperative Interventions	Intra-operative Interventions	Postoperative Interventions
Controlled breathing education	IV infusion of lactated ringers at 30 mL/kg/hr	Practice of controlled breathing with nurse in PACU if PONV occurs
Personal PONV risk factor questionnaire completion with pre-operative nurse	Standard prophylactic ondansetron dose	
Education on intraoperative acupuncture	Prophylactic dexamethasone dose of 0.15 mg/kg for high risk patients prior to anesthesia induction	
Acquire or document refusal of informed consent on intraoperative acupuncture	Stimulation of acupuncture point P6 if informed consent signed in pre-operative area	

The best practice guideline provided to nursing staff, surgeons, anesthesiologists and acupuncturists will include rationales with supporting documentation for the aforementioned

interventions to encourage adoption of these guidelines in the clinical setting. To encourage interdisciplinary collaboration, a perioperative meeting will be held where all relevant personnel will be taught the entire protocol and how the other healthcare members will be a part of the implementation. During this meeting, the interdisciplinary team will have a discussion regarding areas of concern before establishing consensus on the proposed guidelines for the new implementation. The interventions will be added to standing orders for all surgical patients and postoperative patients. Based on the recommendations found in Chapter 3, peri-operative nursing staff will be the drivers of force in implementing this best practice guideline. Peri-operative nurse managers and charge nurses will be responsible for holding a staff meeting educating about the best practice guideline and how it will alter or enhance existing agency specific policies and procedures. All peri-operative nurses will be required to attend or complete a standardized course on controlled breathing exercises prior to teaching and implementing this technique with patients. All peri-operative nurses will be trained on applying pressure to acupoint P6 for correct acupressure intervention. A licensed acupuncturist will be hired to complete all intraoperative acupuncture. If and when the licensed acupuncturist cannot attend surgery, nursing staff trained acupressure of acupoint P6 will complete intraoperative acupressure. All required trainings and continuing education courses associated with this clinical protocol will be provided to nursing staff on the clock while being paid in order to convey the facility commitment to success of the protocol and education of their nursing staff.

The last portion of the “plan” section is to develop a plan to evaluate the effect of the implementation (Institute for Healthcare Improvement, 2017). In order to evaluate the efficacy of the clinical protocol bundle, in a follow up phone call, all patients will be asked a series of questions related to satisfaction including overall comfort level, responsiveness of nursing staff,

and areas that they would like to see changed. On the other end of the spectrum, each nurse will be asked to record the episodes of nausea and vomiting encountered by each patient, the time at which the episodes took place and the severity of the episodes using a standardized scale. The results of both patient satisfaction and nursing documentation will be compiled and analyzed biannually for recurring trends and for future analysis. Additionally, quality and safety monitoring will include review of patient charts and incident reports every two weeks for the first eight weeks. Following the first eight weeks, the data will then be reviewed every two months over a four month period and then quarterly until full implementation has been achieved. By reviewing quality and safety measures more frequently at the beginning of the implementation, the healthcare teams and those implementing this bundle may make adjustments and focus on areas of concern as they proceed.

Do

The "do" portion of the PDSA cycle involves carrying out the implementation, collecting data and information regarding success or problems encountered (Institute for Healthcare Improvement, 2017). In this stage of the cycle, the implementation will be carried out on a small scale in one hospital as previously mentioned. The plan to evaluate change as outlined above will be carried out and analyzed every two weeks for the first eight weeks, then every two months for the following four months, and then quarterly until implementation is complete. By monitoring the care bundle more frequently at the beginning of implementation, adjustments can be made to enhance the long term success and quality of care delivered. Similarly, peri-operative nursing staff will also be asked to complete a survey monthly for the first quarter and then quarterly thereafter through secure email regarding their perception of the success or failure of integrating the guideline into clinical protocol. By evaluating the more frequent responses of nurse surveys

at the beginning of the process, the bundle and standing orders can be adapted to better implement the guideline into clinical protocol. The nursing staff will be asked if they have suggestions for improvement as well as what they believe is working well and can be expanded upon.

Evaluation

Study

The "study" portion of the PDSA cycle involves fully analyzing data collected in previous stages and applying those results (Institute for Healthcare Improvement, 2017). While analyzing the data including both nurse and patient satisfactions with the protocol as well as nurse assessment data on frequency and intensity of PONV episodes, the hypothesis that frequency and severity of PONV will be decreased will be evaluated as well (Institute for Healthcare Improvement, 2017). During the biannual analysis and compiling of data, the current results will be compared to previous data sets to analyze for any changes in data, improvements or worsening of PONV in the facility. In comparing the hypothesis to what actually happened based on the data, the team will begin to understand if their objective was met and if not what happened instead.

Act

The "act" portion of the PDSA cycle involves evaluating where changes need to be made and which specific changes need to be carried out to better reach the objective of the implementation (Institute for Healthcare Improvement, 2017). By pulling conclusions from the "study" section and what the end results were, the team will then develop a plan for improving and implementing alterations to the original protocols. Possible areas to be considered for improvements are duration of acupuncture, doses of dexamethasone and ondansetron and total

fluid volumes to be infused intraoperatively. The conclusions made and plan that was developed in the "act" stage of the initial PDSA cycle will guide the "plan" section of the following PDSA cycle (Institute for Healthcare Improvement, 2017). The PDSA cycle will repeat indefinitely until there is a professional consensus as to the success of the protocol and when all objectives of the protocol are met to reduce the overall severity and incidence of PONV in the first 24 postoperative hours for patients undergoing general anesthesia.

Strengths and Limitations of Honors Thesis

This honors thesis possesses many strengths including an extensive review of literature, a comprehensive analysis of individual recommendations and a concise yet thorough set of recommendations for each modality of management of PONV studied. While PONV is a common and distressing effect many face following surgery, there is still much research needed to fully eradicate the unpleasant phenomenon. While extensive, this honors thesis only brushed the surface of all potential modalities and protocols available to manage PONV and exemplifies the fact that extensive research has yet to be done. The conclusions reached in this thesis are largely generalizable to larger populations as the majority of sources included demographics from a wide variety of patients under general anesthesia. Additionally, the conclusions reached in this honors thesis are clinically applicable and cost effective. All sources included in this thesis were under 10 years old and include the most current and relevant research on the topics of PONV and management thereof.

A final and particularly important strong point of this honors thesis is that it incorporates many integrative nursing principles. The fourth integrative nursing principle that "integrative nursing is person-centered and relationship-based" emphasizes that each patient has a different context of illness that requires nurses develop authentic relationships with patients to tailor their

care (Kreitzer, 2015). The bundled protocol proposed in this thesis takes into account the fact that each patient responds differently to treatment and therefore multiple options and overlapping treatments should be available. Additionally, as each patient may respond differently to different medications, reducing the amount of rescue antiemetics used decreases potential side effects, reduces the use of potentially unnecessary medications, and reduces the cost of treatment both to the patient and the healthcare facility. By treating symptoms before they become extreme and cause further complications, healthcare teams can provide more efficient and proactive care. The cost of the complications of not adequately preventing PONV is increased as the patient stays longer, requires more time and attention, and requires more medications and monitoring. By reducing the incidence of symptoms, this bundled protocol to prevent PONV has the potential to decrease the overall cost of postoperative patients experiencing PONV. The fifth integrative nursing principle that states that "integrative nursing is informed by evidence" is particularly emphasized in this honors thesis (Kreitzer, 2015). Through an extensive literature review with up to date articles, I gathered the most relevant and influential data to propose the bundled intervention outlined above. The second integrative nursing principle states that "human beings have the innate capacity for health and wellbeing" is also represented in this thesis (Kreitzer, 2015). By providing patients with effective modalities of PONV management, the patient is therefore exposed to less potential injury, decrease in quality of life, more efficient rest and therefore are on a faster path to healing and well-being.

This honors thesis possesses several limitations as well as strengths. The thesis was limited in that it was not a systematic review including all literature on the included topics and instead focused on data published within the past 10 years. Many of the articles included in this thesis focused on specific patient populations and surgery types which may limit the

generalizability of their results. An additional limitation stems from the fact that not all studies analyzed in this thesis occurred in Western hospitals and in overseas hospitals with the same standards of care. These foreign hospitals may not be representative of the type of clinical setting that the best practice guideline defined in this thesis will attempt to enhance. While the results are clinically applicable, the integration of acupuncture of acupoint P6 into every operative room for intraoperative treatment could prove difficult. Both training and hiring of certified acupuncturists staffing could be difficult. Not every patient may feel comfortable receiving intraoperative acupuncture and therefore it is possible that not every patient will consent to it. Additionally, depending on the type of surgery and positioning of the patient during surgery, it may be difficult or impossible to access the acupoint P6 for every patient.

Perhaps the greatest limitation of this honors thesis is that very few of the presented studies researched the modalities for PONV management in an integrative way. For example, while each study may have tested a modality while controlling all other variables or types of modalities, there were still other modalities used. Where the use of pharmacotherapies was being tested, each patient still received intraoperative intravenous fluids. Where the use of supplemental oxygen was being tested, pharmacotherapies were still being used. Without the isolation of each modality to be studied, it is nearly impossible to know if this modality alone is sufficient in managing PONV. Integrative nursing focuses on the whole being of the person and takes into account both their mind and body (Ringdahl, 2014). Additionally, an integrative nurse incorporates the least to most intensive treatments available to heal or improve the health of their patients (Ringdahl, 2014). Until each modality presented in this thesis is explored independent of current treatments, it will be impossible to develop an integrative protocol moving from the least to most invasive. The literature presented in this thesis provides strong evidence for the

recommendation of a general protocol and therefore has a long way to go before it can be truly called integrative.

Summary

The purpose of this honors thesis was to develop best practice recommendations to reduce the incidence and severity of PONV within the first 24 postoperative hours in patients who undergo procedures under general anesthesia. Extensive and diverse research has been conducted as to the efficacy of individual and combination modalities however as many as 20-30% of all patients still experience PONV (Cutshall & Van Getson, 2014). This alarming proportion of patients experiencing such an unpleasant phenomenon indicates a lack of accuracy in treatment approaches and failure to prevent PONV from occurring. PONV not only is an unpleasant experience but increases postoperative complications, increases length of stay, increases cost of treatment and increases labor required from nursing staff (Cutshall & Van Getson, 2014). Many of the modalities used to manage and prevent PONV are medications which may be expensive and introduce a host of side effects and adverse reactions. By introducing additional modalities to treat and manage PONV such as intraoperative fluid boluses and acupuncture, many patients may not require or be exposed to additional expensive and potential harmful pharmacologic agents. Extensive research is needed to determine the efficacies of each modality on its own for management of PONV as well how to better identify at risk patients and decrease the amount of postoperative opioid use. The PDSA cycle as outlined in Chapter 4 provides health care settings a tool to evaluate the introduction and adjustments used in relation to the proposed best practice recommendation. Overall, the implementation of the proposed best practice guideline into clinical protocols will reduce the incidence and severity of PONV in the first 24 postoperative hours for patients undergoing procedures under general

anesthesia. The reduction in PONV is one step to fully eradicating PONV and improving postoperative care for patients and healthcare providers alike.

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