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An Educational Module on the Utilization of Haloperidol as a Pharmacological Complement for Postoperative Nausea and Vomiting Prophylaxis in Adult Surgical Patients

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I would like to dedicate this dissertation to my beloved grandmother, Miryan Del Pozo, who may not be present to celebrate my accomplishments, but whose memory lives on in my work. Thank you for giving me the greatest advice to live by every day – “enjoy the life!”

Abstract

Postoperative nausea and vomiting (PONV) commonly influence the perioperative experience of general anesthesia patients. Although current guidelines suggest the use of combination therapy for PONV prophylaxis, there is diminished application in practice. A potentially efficacious and under-utilized medication being studied in combination with anti-emetics is haloperidol. The main foci of this quality improvement project are to assess anesthesia provider knowledge and attitudes regarding utilization of haloperidol for PONV prophylaxis in adult surgical patients. This quality improvement project provides a segue to enhance anesthesia practice by diminishing PONV using haloperidol. The primary methodology of the quality improvement project is to implement an online educational module to anesthesia providers that focuses on the significance of PONV in anesthesia practice and the impact of combination PONV prophylaxis utilizing haloperidol. Qualtrics pre- and post-test surveys were employed to gauge the efficacy of the educational module and to evaluate the influence on anesthesia provider knowledge and attitudes. Findings pointed to a significant increase in anesthesia provider knowledge about haloperidol PONV prophylaxis, and overall attitudes. The results showed an increase in anesthesia provider knowledge and attitudes through implementation of the educational module that presents the utilization of haloperidol as a pharmacological complement for PONV prophylaxis.

Keywords: Postoperative Nausea and Vomiting, Haloperidol, Prophylaxis, Combination Therapy

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Significance of the Problem

Postoperative nausea and vomiting (PONV) is defined as nausea and vomiting that can occur up to 24 hours postoperatively and in the post anesthesia care unit (PACU) where patients recover after surgical procedures.[1] In the perioperative setting, PONV is a potential risk factor for all patients who opt for general surgery that involves utilization of anesthesia.[1-2] Throughout the years, a multitude of literature has pointed to promising PONV treatments that are still implemented today.[3] Although many treatments have shown to be efficacious in treating PONV, research has fallen short of identifying a definitive gold standard for PONV management and prophylaxis that includes haloperidol.[3]

With the persistent problem of PONV, healthcare systems and patients have had to face increased costs, decreased patient satisfaction, adverse surgery outcomes, prolonged hospital stays, and delayed PACU discharge.[2,4-5] Combination therapy incorporating haloperidol for PONV prophylaxis may contribute to a profound and positive transformation in the perioperative arena.[6-9] Guidance on the aforesaid subject may better equip anesthesia providers to combat the negative outcomes prompted by PONV and diminish the occurrence of PONV overall.[10] In this dissemination, the investigator aims to answer the following question: (P) In adult surgical patients (I) does an educational module on the utilization of haloperidol as a pharmacological complement for PONV prophylaxis (C) versus no educational module (O) increase anesthesia provider knowledge and attitude in implementing haloperidol as an adjunct treatment in the management of PONV? The goal of this quality improvement (QI) project is to improve anesthesia provider knowledge and attitude of PONV prophylaxis with an education module that focuses on the use of haloperidol in combination PONV prophylaxis as modeled by an algorithm

endorsed by an international panel of professional societies, including the American Society of Anesthesiologists (ASA).

Background

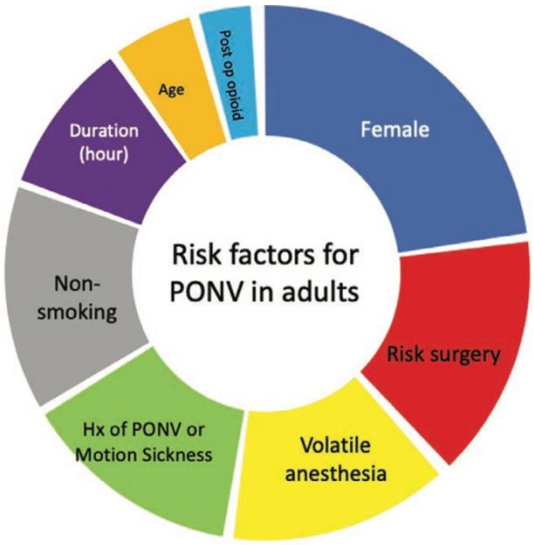
The area in the brain associated with interpreting stimuli that cause nausea and vomiting is found in the medulla.[11] Various pathways provide input to the medulla emetic center such as the following: the vestibular apparatus, chemoreceptor trigger zone (CTZ), visceral afferent innervation of the gastrointestinal (GI) tract, solitary tract nucleus, cerebellum, and the cerebral cortex.[11-12] Of these pathways, one of the major characteristics of the CTZ is its connection to drugs and toxins circulating the body due to its location outside of the blood-brain barrier and in the fourth ventricle.[11] Each of the aforesaid pathways involved in nausea and vomiting are regulated by neurotransmitters and receptors.[11] The vomiting reflex is found to be stimulated by activation of receptors in the emetic center such as neurokinin-1 (NK-1), serotonin type 3, acetylcholine (muscarine), dopamine, opioid, and histamine receptors.[11,13]

Various anesthetic, patient, and surgical factors help predict the potential incidence and severity of PONV.[1-2,14] Anesthetic PONV triggers depend on the utilization of volatile anesthetics, nitrous oxide, opioid administration, anesthetic duration, and anesthetic technique.[1] Particularly, patients most at risk are those who have received inhalational anesthetics and opioids.[2] It has been found that commonly used opioids, such as fentanyl and morphine, contribute to PONV independent of other factors.[2] Research demonstrates that early PONV, 0 – 2 hours postoperative, is mostly attributed to use of inhalational agents and delayed PONV has been linked to opioid use 2 - 24 hours postoperative.[14] General anesthetic technique has been found to cause more PONV than regional anesthesia, and despite the lower occurrence of PONV

with a total intravenous anesthetics (TIVA) technique, PONV still occurs.[1] Other notable PONV triggers increasing its incidence are nitrous oxide use and longer anesthetic exposure.[1]

Additionally, the type of surgery and surgical duration increase PONV risk related to surgical factors.[1] Surgeries linked to the highest PONV incidence are longer procedures and those of gynecological, breast, ophthalmic, otorhinolaryngological, intra-abdominal, and laparoscopic nature especially cholecystectomy.[1,6] In combination with anesthetic and surgical factors previously mentioned, patient factors, such as genetics, PONV history, gender, age, and smoking status, also play a role in the incidence of PONV.[1] The greatest PONV predictors in order of influence are female gender, previous PONV history, first-degree relatives with PONV history, non-smoking status, motion sickness history, and those who are less than 50 years old.[1] Specific to children, PONV risk is increased by strabismus surgery, procedures lasting longer than 30 minutes, age greater than 3 years old, and PONV family history.[8] The International Anesthesia Research Society demonstrates a relative depiction of intraoperative and postoperative PONV risk factors amongst adults in figure 1, where the size of each segment is proportional to the odds ratios of PONV associated with each risk factor.[8]

Figure 1. ***Adult Intraoperative and Postoperative PONV Risk Factors***



Currently, many medications are available in the anesthesia provider's PONV prophylaxis drug armamentarium. Literature classifies PONV medications as older generation, newer generation, and non-traditional anti-emetics.[6] The newer generation anti-emetics include serotonin receptor and NK-1 receptor antagonists.[6]

Serotonin receptor antagonists are known for ligand binding and blocking the serotonin 5-HT3 receptor in the GI tract vagal afferents and the CTZ.[6] The most used serotonin receptor antagonist is ondansetron; however, others with similar characteristics are dolasetron, tropisetron, and granisetron.[6] Dizziness, headache, flushing, QT prolongation, and elevated liver enzymes are potential side effects of serotonin 5-HT3 receptor antagonists.[6,13] NK-1 receptor antagonists, such as aprepitant, are known to block NK-1 receptors in the peripheral nervous system, area postrema, and nucleus tractus solitarius preventing substance P, the natural ligand, from binding.[8,12] While the NK-1 receptor blocker, aprepitant, shows promise in PONV prevention, other medications in this category, such as casopitant and rolapitant, have not been approved for use.[8] Unlike the serotonin 5-HT3 receptor antagonists in the newer generation anti-emetics, aprepitant does not prolong QT and fails to cause sedation like some other anti-emetic medications.[13] Corticosteroids have been classified as non-traditional anti-emetics; however, their mechanism of action in this respect is unknown.[6] There is suspicion that the anti-inflammatory and endorphin releasing properties of corticosteroids may contribute to their anti-emetic effect.[6] Dexamethasone is the most used corticosteroid for PONV and is not associated with side effects at doses used for PONV prevention.[6]

Older generation anti-emetics include phenothiazines, antihistamines, anticholinergics, benzamides, and butyrophenones.[6] Phenothiazines, such as chlorpromazine, promethazine, prochlorperazine and perphenazine, are responsible for antagonizing dopamine D2 receptors in

the CTZ.[6] Side effects of phenothiazines are sedation, restlessness, hypotension, neuroleptic malignant syndrome (NMS), and anticholinergic effects.[6] Dopamine receptor blocking agents are also capable of precipitating extrapyramidal symptoms (EPS), which can present as abnormal muscle tone and movements.[15] Akathisia, tardive dyskinesia, parkinsonism, and dystonia are grouped together as physical manifestations of EPS that can be described as tremors, rigidity, and bradykinesia.[15] The physical manifestations of EPS have been tied to psychological symptoms such as cognitive impairment, apathy, and dysphoria.[15]

Antihistamines, such as diphenhydramine, dimenhydrinate, hydroxyzine, and cyclizine, affect the nucleus of the solitary tract histamine H1 receptors and the vestibular apparatus by antagonizing acetylcholine receptors.[6] Side effects of antihistamines include dry mouth and sedation.[6] Anticholinergics, such as scopolamine and atropine, work on the pons and cerebral cortex blocking cholinergic and muscarinic receptors in the central nervous system.[6] Blurred vision, dry mouth, mydriasis, hallucinations, sedation, urinary retention, disorientation, confusion, and cholinergic syndrome are potential side effects of anticholinergics.[6] Among the benzamides, metoclopramide is administered the most and is known for its prokinetic properties.[6] Metoclopramide specifically antagonizes GI tract dopamine D2 receptors and affects the same receptors in the area postrema and CTZ.[6] Side effects associated with benzamide use include restlessness, sedation, hypotension, bradycardia, tachycardia, and EPS.[6]

Butyrophenones, such as haloperidol and droperidol, are recognized to work at the area postrema and CTZ as dopamine D2 receptor antagonists.[6] Haloperidol has been underutilized in anesthesia; however, droperidol provided a sufficient anti-emetic treatment before it was labeled with a black box warning due to sudden cardiac death.[6] Butyrophenones rarely cause EPS and have been associated with QT prolongation, torsades de pointes, hypotension, sedation, NMS,

urinary retention, nightmares, and visual disturbance.[6,8,13,16] As haloperidol is the featured focus of this quality improvement project, the topic requires further dissemination on its pharmacological and biochemical qualities. Upon the synthesis of haloperidol in 1958 by Janssen Pharmaceutical research laboratories, the original aim was for use as a neuroleptic medication.[17] The birth of haloperidol contributed to the knowledge base of psychiatry through understanding of neurobiology and psychopharmacology.[17] The initial indications for haloperidol use were for hallucinations, delirium, and psychomotor related diseases.[18]

When researchers studied haloperidol's properties on dogs in 1976, it was found that it has a long duration of action of 64 hours when administered via oral and subcutaneous routes.[17] Equipotency of both oral and subcutaneous routes of haloperidol administration was found to occur after the fourth hour at 0.03 milligrams (mg)/kilogram (kg), and research supports oral absorption and potency at this dose.[17] Haloperidol's onset of action was shown to differ based on route of administration; the onset of the subcutaneous route was faster than the oral route, which peaked after four hours.[17] A further study showed that haloperidol is a typical neuroleptic that exhibits sedative and alpha-adrenergic inhibiting properties, unlike atypical neuroleptics.[17] From a biochemical standpoint, it first became known that haloperidol blocks dopamine receptors when the 1976 study showed inhibition of dopamine production on cyclic adenosine monophosphate (cAMP).[17]

When haloperidol's neuroleptic profile was studied, researchers explored the anti-nausea and anti-emetic properties of a single 1 mg intramuscular injection of haloperidol in a double-blind placebo-controlled trial in 1975 involving a total of 62 patients.[19] In the study by Barton et al,[19] male and female subjects had surgical procedures ranging from tubal ligation to mandibular reconstruction and received anesthetic agents available during this period such as cyclopropane,

sodium thiopental, nitrous oxide, halothane, ether, and fluroxene. Thirty minutes after haloperidol administration, 71% of subjects did not experience nausea and 83% failed to vomit, while 29% of placebo patients experienced vomiting and 20% expressed nausea, thus showing haloperidol's superior treatment of PONV over placebo.[19] After an hour, subjects in the haloperidol group did not experience any vomiting.[19] Despite the known side effects of haloperidol seen at high doses, subjects in the Barton et al[19] study who received a low dose of haloperidol did not experience hypotension or EPS.

Since the 1970s, more research has been conducted which focuses on haloperidol and its ability to prevent PONV. In 2005, the American Association of Nurse Anesthetists (AANA) journal featured a publication by Smith and Wright that highlighted haloperidol's role in PONV prophylaxis.[16] After a review of prior studies, it was established that haloperidol's PONV prophylactic potency began within 30 minutes of administration and its duration of action is 4 hours.[16] Smith and Wright[16] also informed that efficacious dosages of haloperidol for PONV prophylaxis were 0.015 mg/kg IV and 0.007 mg/kg IM, where the IM route was more efficacious. At that time, studies pointed to PONV antiemetic doses to be between 0.5 mg to 1 mg.[16] According to Smith and Wright,[16] haloperidol use was linked to the presentation of adverse effects previously mentioned when it was given at high doses in psychiatric practice, such as 35 mg or more within a 24-hour period. At low doses used for PONV, the risk of adverse effects is minimal.[16] Despite the low risk, it is best advised to avoid haloperidol in patients with QT prolongation, congestive heart failure, acute/chronic dysrhythmias, electrolyte disturbances, cardiac hypertrophy, acute cardiac syndromes, Parkinson's disease, and NMS.[16] Additionally, patients taking monoamine oxidase inhibitors and tricyclic antidepressants should refrain from taking haloperidol.[16]

In 2008, Wang et al[18] studied the PONV efficacy of haloperidol in 150 women who had undergone ambulatory laparoscopic surgery that involved the same general anesthetic with tracheal intubation and administration of fentanyl, propofol, rocuronium, desflurane with oxygen, neostigmine, and atropine. Wang et al,[18] conducted a double-blind randomized placebo-controlled study in women who received 1 mg of IV haloperidol, 0.625 mg of IV droperidol, or a saline placebo. As a result, subjects who received haloperidol and droperidol demonstrated a similar incidence of PONV at 31% and 32% respectively, which was lower than the placebo group at 62%.[18] Additionally, subjects in the haloperidol and droperidol groups required less rescue anti-emetics than those in the placebo group who required 4 mg of ondansetron.[18] At such a low dose of haloperidol, subjects did not experience QT prolongation, EPS, or sedation.[18]

Yang et al[20] explored the PONV prevention efficacy of haloperidol and compared the timing of administration during the perioperative period in a randomized, double-blind study of women undergoing plastic, gynecologic, breast and thyroid surgeries. Ninety-four women participated in this study who had a history of PONV and/or motion sickness, were non-smokers, and were classified as a physical status score of I or II by the ASA.[20] Subjects in the Yang et al[20] study received 2 mg of haloperidol IV 30 minutes before the termination of surgery or during anesthetic induction and had undergone general anesthesia with tracheal intubation using fentanyl, propofol, rocuronium, sevoflurane with oxygen, neostigmine, and atropine. Findings yielded no difference in the anti-emetic efficacy of haloperidol when administered at different times, which was suspected to be due to haloperidol's long elimination half-life of 12 – 35 hours that typically averages 16 hours, which is unlike droperidol's shorter elimination half-life.[20] At such low haloperidol doses, subjects did not experience significant sedation nor cardiac arrhythmias.[20]

Scope of the Problem

Despite the availability and use of current treatments, PONV affects over 25 – 30% of surgical patients.[6] When considering surgical patients at risk of experiencing PONV, the incidence of PONV has been found to be as high as 80%.[1-2] Although the severity of PONV has decreased, the incidence has not.[6] Recently, research has found that the incidence of PONV has been amplified by the growth observed in ambulatory surgery.[21] Elvir et al[21] also brings to the forefront that pressures promoting timely discharge and mobilization after surgery have been catalysts in the PONV issue.

In the adult population, the PONV incidence has been noted to be the highest at 40 – 77% after laparoscopic procedures.[6] Otorhinolaryngological and ophthalmic procedures among adults have been tied to a 71% incidence of PONV, while intra-abdominal surgeries came in close at 70%.[6] Additionally, gynecological surgeries ranked a PONV incidence of 58% and breast surgeries were linked to a 50 – 65% PONV occurrence.[6] In the pediatric population, the patients who demonstrated the highest risk for PONV at 85% were those who had strabismus surgery.[6] Pediatric patients who experienced middle ear surgeries and tonsillectomies were also considered high risk for developing PONV.[6]

Consequences of the Problem

Although PONV is non-fatal, it is notorious for straining healthcare systems through increased costs and causing undesirable health outcomes that have led to decreased patient satisfaction.[5,14] According to Habib and Gan,[6] PONV is ranked in the top 10 most unfavorable outcomes after surgery. Unpleasant symptoms associated with PONV contributing to considerable patient morbidity and distress include esophageal rupture, wound dehiscence,

aspiration, decreased oral intake, electrolyte disturbances, dehydration, bleeding, venous hypertension, and airway compromise.[1,5,11,14]

Among patients who have experienced PONV, many have been met with delayed PACU discharge.[1-2,6-7,11] Patients who have succumbed to severe PONV have shown to be subjected to preventable hospital admission that prolonged hospital stays.[2,5-7,11] Researchers found that the hospital length of stay postoperatively increased by 25% in general anesthesia patients and 79% in monitored anesthesia care (MAC) patients who experienced protracted PONV.[6]

The overall effect of PONV has contributed to higher costs associated with an increased demand for nursing labor and hospital resources.[12] The healthcare costs accrued due to lengthy hospital stays and delayed PACU discharge secondary to PONV were discovered to surpass the cost of prophylactic anti-emetic treatment.[1] Wang et al[18] pointed out that the typical cost of haloperidol in Taiwan is $0.30 in US dollars that is significantly less than ondansetron, which is commonly used as a rescue anti-emetic and can cost as much as $7.47 in US dollars.

While healthcare costs are significant, delayed PACU discharge, hospital admission, and adverse surgery outcomes have also led to decreased patient satisfaction among those affected by PONV.[1,12] Research has demonstrated that PONV prophylaxis has been tied to improved patient satisfaction and shows to be cost-effective especially in high-risk patients.[12] Surgical patients who were studied valued PONV prevention so much that they were willing to pay $56 - $100 to circumvent the unfavorable effects of PONV with a hypothetical anti-emetic that provided a complete response in PONV prophylaxis.[4]

Knowledge Gaps

According to Eberhart et al,[22] no single drug is credited with the power to diminish PONV to a tolerable level. Considering the high incidence and persistence of PONV, the use of a

sole agent for PONV prevention has been advised against due to the potential for positive outcomes with a combination approach to PONV prophylaxis.[7] Therefore, research advocates for the utilization of combination therapy for PONV prophylaxis with the understanding that antagonizing multiple receptors associated with PONV can provide superior PONV prevention in surgical patients.[7-9,23] Although there is significant literature available today that addresses PONV, the utilization of PONV combination therapy in surgical patients is lacking in practice.[9] Dewinter et al[9] published that there is limited knowledge of PONV guidelines and adherence to published guidelines is not consistent. In efforts to address the adverse effects of nausea and vomiting along with decreased compliance, PONV algorithms were simplified by Dewinter et al[9] researchers with the goal of ultimately reducing the incidence of PONV.

Proposal Solution

In 2018, the British Journal of Anesthesia delineated a PONV algorithm depicted in figure 2 that recommended using up to three anti-emetics, droperidol, ondansetron, and dexamethasone, in PONV prophylaxis depending on PONV risk stratification.[9] The British Journal of Anesthesia simplified this algorithm, which is highlighted in figure 3. Following this, the International Anesthesia Research Society expanded on previously published iterations on PONV prophylaxis and suggested guidelines in 2020 that modeled haloperidol's medication class in PONV combination therapy.[8] The most recent PONV practice guideline update published by the International Anesthesia Research Society is endorsed by multiple international professional societies, including the ASA and the AANA. [8] Additional anesthesia experts supporting the PONV practice guidelines published by the International Anesthesia Research Society include the following societies: the American Society for Enhanced Recovery, the American Society of Health Systems Pharmacists, the American Society of Peri Anesthesia

Nurses, the American Academy of Anesthesiologist Assistants, the American College of Clinical Pharmacy, American College of Clinical Pharmacy Perioperative Care Practice and Research Network, the Australian Society of Anesthetists, the Brazilian Society of Anesthesiology, and the Chinese Society of Anesthesiology.[8]

The guidelines previously mentioned suggest utilization of anti-emetics based on risk stratification similar to the British Journal of Anesthesia.[8-9] Per the International Anesthesia Research Society, the recommended guidelines for PONV management in adult surgical patients suggests administering two agents if exhibiting one to two risk factors for PONV and giving three to four agents if there are greater than two risk factors.[8] The recommended prophylactic PONV agents highlighted for adult use by the most recent algorithm in 2020 are meant to be selected from different drug classes, which include the following: 5-HT3 receptor antagonists, antihistamines, corticosteroids, dopamine antagonists, NK-1 receptor antagonists, and anticholinergics highlighted in figure 4.[8] Additional prophylactic approaches are also considered in the ASA endorsed PONV adult algorithm, such as propofol anesthesia and non-pharmacologic measures like acupuncture.[8]

Among children, the PONV prophylaxis guideline published by the International Anesthesia Research Society also involves risk stratification similar to that of adults except recommended agents are 5-HT3 antagonists and dexamethasone as depicted in figure 5.[8] According to Gan et al,[8] a child with no risk factors is classified as low risk and may require one agent, 5-HT3 antagonist or dexamethasone, all the while, a child exhibiting one to two risk factors, medium risk, suggests combining use of dexamethasone and a 5-HT3 antagonist. Among high-risk children who exhibit greater than three risk factors, the International Anesthesia Research Society recommends combining a 5-HT3 antagonist, dexamethasone, and TIVA.[8]

Following prophylaxis with dexamethasone and/or 5-HT3 antagonists in children, it is suggested to utilize more agents from different classes as needed for PONV rescue treatment.[8] The International Anesthesia Research Society summarizes common combinations of anti-emetics recommended for PONV pharmacologic combination therapy for adults and children in figure 6.[8]

Figure 2. ***British Journal of Anesthesia Risk Stratified PONV Algorithm***

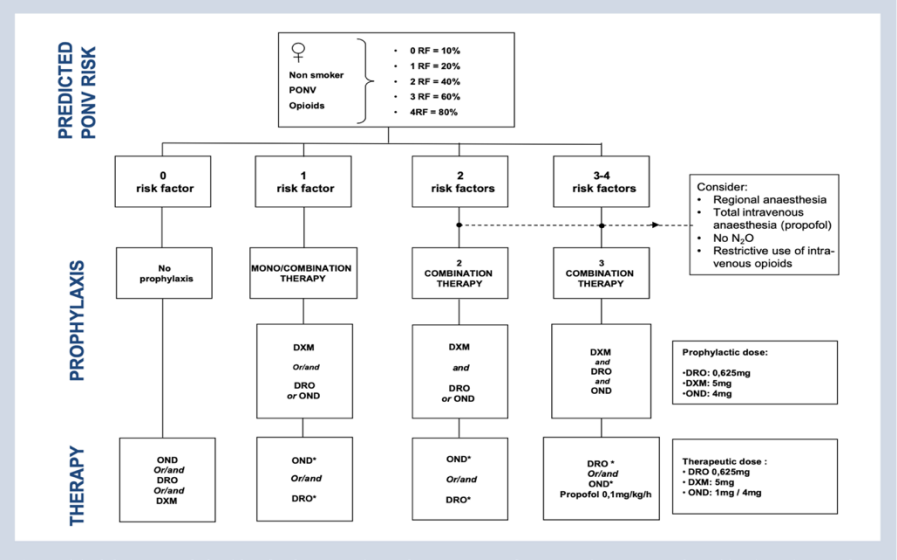


Figure 3. ***British Journal of Anesthesia Simplified PONV Algorithm***

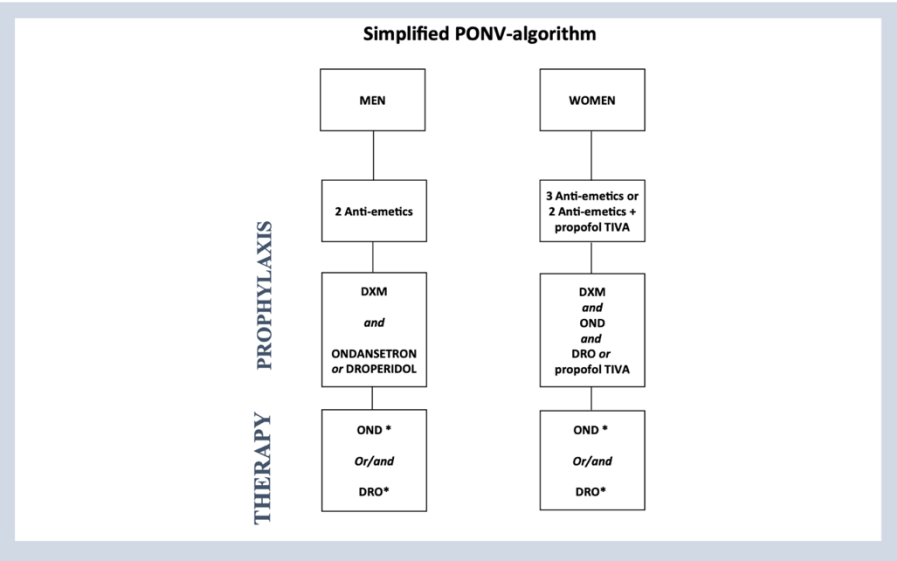


Figure 4. ***International Anesthesia Research Society PONV Guidelines for Adults***

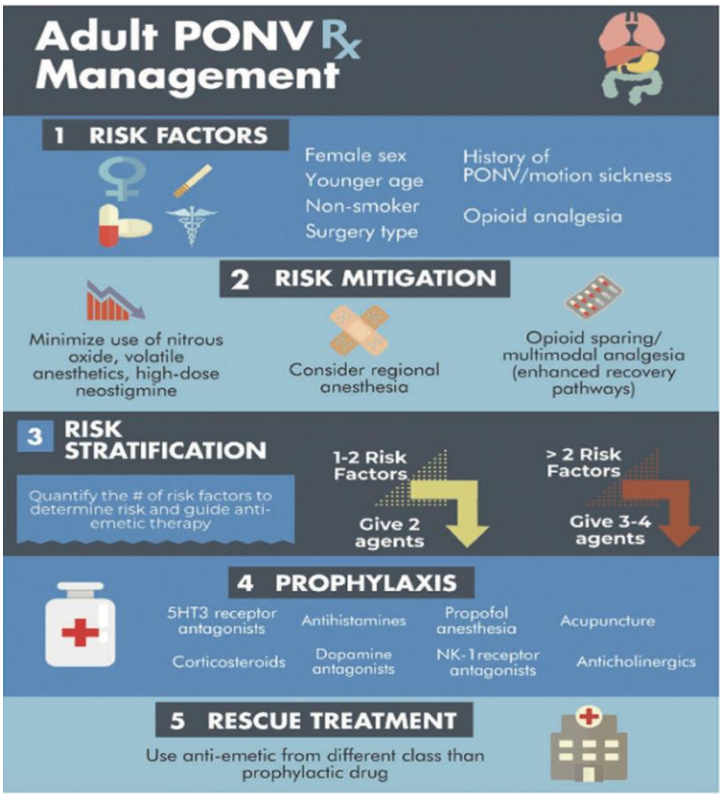


Figure 5. ***International Anesthesia Research Society PONV Guidelines for Pediatrics***

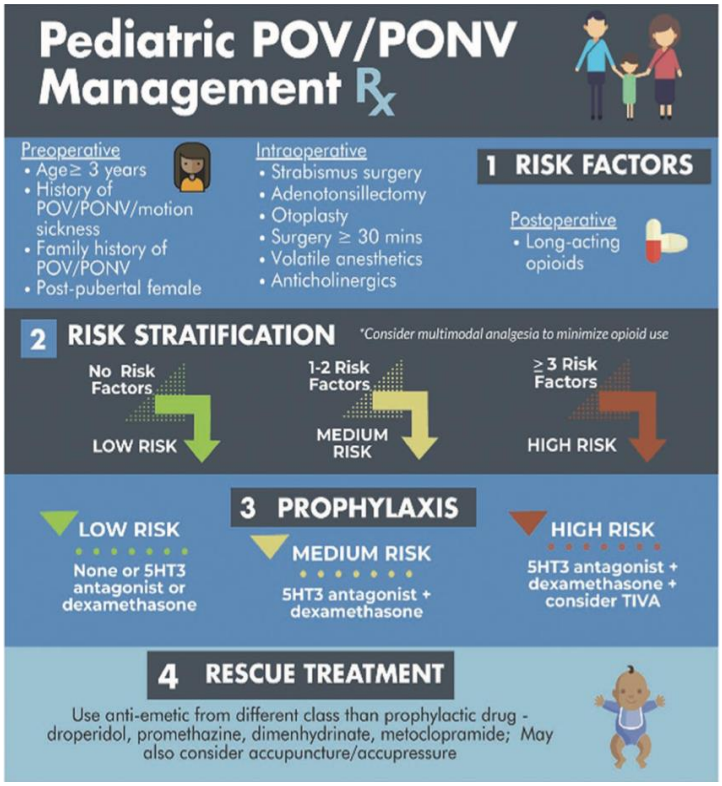
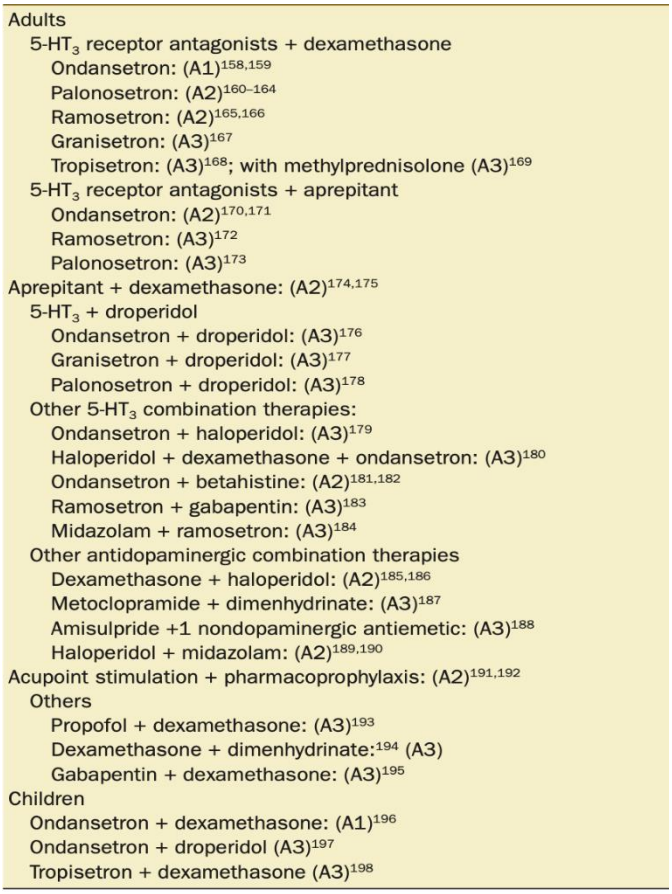


Figure 6. ***International Anesthesia Research Society PONV Medication Combinations***



Adults
- 5-HT_3 receptor antagonists + dexamethasone
  - Ondansetron: (A1)[158,159]
  - Palonosetron: (A2)[160–164]
  - Ramosetron: (A2)[165,166]
  - Granisetron: (A3)[167]
  - Tropisetron: (A3)[168]; with methylprednisolone (A3)[169]
- 5-HT_3 receptor antagonists + aprepitant
  - Ondansetron: (A2)[170,171]
  - Ramosetron: (A3)[172]
  - Palonosetron: (A3)[173]

Aprepitant + dexamethasone: (A2)[174,175]
- 5-HT_3 + droperidol
  - Ondansetron + droperidol: (A3)[176]
  - Granisetron + droperidol: (A3)[177]
  - Palonosetron + droperidol: (A3)[178]
- Other 5-HT_3 combination therapies:
  - Ondansetron + haloperidol: (A3)[179]
  - Haloperidol + dexamethasone + ondansetron: (A3)[180]
  - Ondansetron + betahistine: (A2)[181,182]
  - Ramosetron + gabapentin: (A3)[183]
  - Midazolam + ramosetron: (A3)[184]
- Other antidopaminergic combination therapies
  - Dexamethasone + haloperidol: (A2)[185,186]
  - Metoclopramide + dimenhydrinate: (A3)[187]
  - Amisulpride +1 nondopaminergic antiemetic: (A3)[188]
  - Haloperidol + midazolam: (A2)[189,190]

Acupoint stimulation + pharmacoprophylaxis: (A2)[191,192]
- Others
  - Propofol + dexamethasone: (A3)[193]
  - Dexamethasone + dimenhydrinate:[194] (A3)
  - Gabapentin + dexamethasone: (A3)[195]

Children
- Ondansetron + dexamethasone: (A1)[196]
- Ondansetron + droperidol (A3)[197]
- Tropisetron + dexamethasone (A3)[198]

Abbreviation: 5-HT_3, 5-hydroxytryptamine 3.

Although haloperidol is not FDA approved specifically for PONV prevention, the black box warning placed on droperidol has led to its declined use and there has been an increased interest in haloperidol utilization as an alternative.[8-9] Although suggested guidelines and algorithms exist, there is no gold standard combination PONV treatment including haloperidol that is being followed consistently to lower the PONV incidence below the current occurrence in all surgical patients.[8-9] Taking this into consideration, extensive research highlights the value of haloperidol in PONV prophylaxis and combination PONV therapy. Among the suggested PONV prophylaxis drug combinations supported by the international panel of anesthesia experts in 2020, haloperidol is found to be a promising option when grouped with ondansetron and/or

dexamethasone.[8] The quality of evidence used to validate the aforementioned pharmacological therapies of PONV agents is high, which suggests supportive literature exists for the basis of this algorithm.[8] According to recent recommendations by Gan et al,[8] the most efficacious dose of IV or IM haloperidol ranges between 0.5 to 2 mg during the perioperative period. Gan et al[8] found that when 1 mg of haloperidol was given after the induction of anesthesia, there were no EPS reported and at this dose, 4 mg of ondansetron was not superior in PONV prophylaxis at 4 and 24 hours following administration. Gan et al[8] also showcased that although there was an associated increase in sedation, the PONV risk was no different in PACU and over the course of 24 hours if 2 mg of haloperidol was administered at the end of surgery or at induction.

In 2007, Rüsch et al[23] explored the additive effect of anti-emetics used in combination with other anti-emetic pharmacological treatment in a randomized study. Researchers in the Rüsch et al[23] study found that dexamethasone enhanced the PONV prophylaxis effect of haloperidol and dolasetron. Among 242 patients undergoing elective procedures under general anesthesia, both IV haloperidol and dolasetron showed similar efficacy in PONV prevention and demonstrated superior effect when either was combined with dexamethasone versus when used as sole agents.[23]

Dagtekin et al[24] conducted a randomized and double-blinded study in 2009 that explored haloperidol used as a sole agent for PONV versus haloperidol used in combination with ondansetron. In the Dagtekin et al[24] study, 60 patients undergoing strabismus or retinal surgery received 10 micrograms (mcg)/kg of haloperidol with 0.1 mg/kg of ondansetron or solely 10 mcg/kg of haloperidol. Findings published by Dagtekin et al[24] reported that haloperidol used in combination therapy provided better PONV results than when used alone.

Despite the saturation of literature, supportive evidence provided still validates haloperidol's essential role in PONV prophylaxis in adult surgical patients when integrated with combination anti-emetic therapy. The efficacy of haloperidol in combination with pharmacological therapy among adult surgical patients will create a paradigm shift in the knowledge and attitude of PONV prophylaxis among anesthesia providers in utilizing the empirical evidence for best practice in the prevention of PONV.

Summary of the Literature

Eligibility Criteria

Selection of studies for this literature review required a more expansive search due to saturation of research. Despite search limitations, inclusion and exclusion criteria were modified to generate sufficient literature with guidance from context experts. Meta-analyses, literature reviews, and systematic reviews were considered as exclusion criteria for this dissemination. Parameters considered as inclusion criteria included literature published within the past fourteen years that was obtainable as full text and followed a randomized clinical trial design. Primary studies selected centered on the efficacy of haloperidol for PONV prophylaxis in combination therapy and as a sole agent. The Florida International University (FIU) library facilitated the search by providing access to most databases utilized. Complemented by Boolean operators, keywords used in this search included variations and combinations of the following: Haloperidol, Postoperative Nausea and Vomiting, Prophylaxis, and Combination Therapy.

Information Sources

MEDLINE (ProQuest) and the Cumulative Index to Nursing and Allied Health Literature (CINAHL) were the primary databases employed. The Directory of Open Access Journals (DOAJ) accessed via Florida International University (FIU) Library services and the Anesthesia

& Analgesia Journal also provided a supplemental search avenue for literature not obtained via CINAHL and MEDLINE.

Search Strategy

Initially, the keyword search in MEDLINE and CINAHL included the following terms: (haloperidol OR haldol) AND (PONV OR postop* nausea and vomiting) AND (prophylaxis or prevention) AND (combination therapy OR combination). Consequently, both databases yielded a total of 33 articles, 7 from CINAHL and 26 from MEDLINE. Upon modification of the publication time frame to range from 2008 – 2021, the search was refined yielding a total of 27 articles. Four duplicate articles were excluded resulting in 23 articles left for analysis. Of the remaining 23 articles, further investigation led to exclusion of 17 articles that did not meet inclusion criteria. Research articles excluded did not meet inclusion criteria based on the type of publication, meta-analysis or systematic review, or failing to include haloperidol in the studies. A total of 6 articles were selected for use from CINAHL and MEDLINE that focused on haloperidol's use in combination with other anti-emetics.

Additionally, a search within the Directory of Open Access Journals (DOAJ) – Not for CDI Discovery, and the official journal of the International Anesthesia Research Society, Anesthesia & Analgesia, was done. The DOAJ search included using the following terms: (haloperidol OR haldol) AND (PONV OR postop* nausea and vomiting). As a result, the DOAJ yielded over 866 articles. When search parameters were modified to include more recent literature from 2019 – 2021 that was peer reviewed and available online, the DOAJ yielded 179 articles. Of the 179 articles generated by the DOAJ, one article met inclusion criteria that discussed the PONV efficacy of haloperidol and was a randomized controlled trial. The search within Anesthesia & Analgesia also included using the following terms: (haloperidol OR haldol)

AND (PONV OR postop* nausea and vomiting). As a result, Anesthesia & Analgesia yielded 19 articles. Of the 19 articles generated, one article met inclusion criteria that discussed the PONV efficacy of haloperidol and was a randomized controlled trial.

Study Characteristics

The eight articles identified for analysis studied fundamental topics in question. The primary subject involving PONV prophylaxis using haloperidol in combination therapy was explored by Benevides et al[25] in 2013, Joo et al[26] in 2015, Chaparro et al[27] in 2010, Chu et al[28] in 2008, Wang et al[29] in 2012, Grecu et al[30] in 2008, and Feng et al[31] in 2009. These researchers aimed to investigate the role of combined PONV therapy integrating haloperidol used for varying surgical procedures amongst adults. One article studied haloperidol used in combination with ondansetron and dexamethasone, four articles focused on assessing the PONV efficacy of haloperidol when used with dexamethasone, and two articles investigated haloperidol in combination with ondansetron. The eighth article by Dağ et al,[32] focused on analyzing the PONV efficacy of haloperidol used as a sole agent in adult female surgical patients in 2019. Overall, all studies examined the adult population during their postoperative experience following general anesthesia, included haloperidol in the PONV prophylactic treatment, and were randomized clinical trials.

Results of Individual Studies

Effect of Low-Dose Haloperidol as a Sole Agent on PONV

Among the most recently published literature on PONV in 2019, Dağ et al[32] sought to find the most effective dose of haloperidol that provided the least amount of side effects and yielded the best PONV prevention. Supplemental research by Dağ et al[32] also aimed to explore patient satisfaction who participated in the study. Dağ et al[32] study meets criteria for

classification as experimental with good, level I evidence due to randomized assignment of treatment groups and utilization of a traditional control group. All participants in this study, subjects, anesthesiologists, and postoperative evaluators, were also blinded to the allocation of treatment groups, which diminished bias.[32] Dağ et al[32] included 250 female patients who were scheduled for laparoscopic abdominal hysterectomy, between 19 and 70 years old, and were given a physical classification score of ASA I – II. Subjects excluded from this study were those who were allergic to opioids, had a nasogastric tube for 24 hours prior to surgery, were given anti-emetics 24 hours before surgery, needed a large intestinal resection, had a haloperidol contraindication, or had a history of cranial, cardiac, renal, hepatic, or lung disease.[32] Participating subjects were randomly assigned to five groups that received different doses, 0.25 mg, 0.5 mg, 1 mg, or 2 mg, of haloperidol parenterally or the saline placebo.[32] All patients received midazolam preoperatively and had undergone general anesthesia with tracheal intubation that involved administration of propofol, fentanyl, rocuronium, sevoflurane, nitrous oxide, oxygen, neostigmine, and atropine intraoperatively.[32] Additionally, participants received 30 mg of morphine for PCA at the termination of surgery.[32] Data was collected from all subjects beginning at 30 minutes postoperatively and was followed by continued observation for 24 hours; researchers documented outcomes hourly for the first 4 hours, every 2 hours until the sixth hour, every 6 hours until the twelfth hour, and then every 12 hours until 24 hours postoperatively.[32] During this time, researchers recorded vitals, side effects, sedation level, patient satisfaction, and need for anti-emetics.[32] Researchers utilized mean, standard deviations, normality tests using Kolmogorov-Smirnov test with Lilliefors correction, Kruskal-Wallis test, Mann-Whitney U test, Monte Carlo test, and Chi-square test to analyze data.[32] Data collected was further analyzed at a 95% confidence level using version 17.0 of Statistical Package for the

Social Sciences (SPSS) for windows.[32] The incidence of nausea differed 2 hours postoperatively and was recorded as statistically significant at $P > 0.008$; 28% of patients in group V given 0.25 mg of haloperidol, 14% of patients in group IV given 0.5 mg of haloperidol, 14% in group III given 1 mg of haloperidol, 4% of patients in group II given 2 mg of haloperidol, and 26% of patients in group I given the placebo had nausea.[32] There was also a statistically significant difference at $P = 0.000$ of nausea incidence between 2 and 24 hours after surgery; 28% of patients in group V given 0.25 mg of haloperidol, 6% of patients in group IV given 0.5 mg of haloperidol, 2% in group III given 1 mg of haloperidol, 4% of patients in group II given 2 mg of haloperidol, and 18% of patients in group I given the placebo had nausea.[32] Two hours postoperatively, researchers observed a statistically significant difference at $P = 0.009$ among groups regarding the incidence of vomiting; 16% of patients in group V given 0.25 mg of haloperidol, 10% of patients in group IV given 0.5 mg of haloperidol, 6% in group III given 1 mg of haloperidol, 0% of patients in group II given 2 mg of haloperidol, and 20% of patients in group I given the placebo experienced vomiting.[32] Between 2 and 24 hours after surgery, groups did not show a statistically significant difference at $P = 0.218$ in regards to the incidence of vomiting.[32] Ultimately, there was a statistically significant difference among treatment groups; the placebo group experienced the highest anti-emetic need at 40% while the subjects treated with haloperidol required fewer rescue anti-emetics.[32] According to Dağ et al,[30] 6% of participants who received 2 mg of haloperidol in group II, 8% of participants who received 1 mg of haloperidol in group III, 14% of participants who received 0.5 mg of haloperidol in group IV, and 28% of participants who received 0.25 mg of haloperidol in group V needed an additional anti-emetic, which was statistically significant at $P < 0.05$.[32] The primary findings from the Dağ et al[32] study highlighted that the optimal and efficacious dosages of parenteral haloperidol for

PONV range from 0.5 mg to 2 mg, despite literature in 2005 by Smith and Wright that presented a narrower range from 0.5 mg to 1 mg.[16] Participants in group II who received the highest dose of haloperidol of 2 mg experienced the highest level of patient satisfaction that was also statistically significant at $P < 0.05$.[32] Researchers also found that at such low doses no QT interval prolongation or arrhythmias were observed, and participants did not experience differing levels of sedation or variation of vitals at all doses.[32]

Combined Effect of Haloperidol, Ondansetron, and Dexamethasone on PONV Versus Sole Use of Ondansetron or Dexamethasone with Ondansetron

While the Dağ et al[32] study focused on haloperidol's role in PONV as a sole agent, further data on the subject can be found in the 2013 study by Benevides et al[25] that considered other anti-emetics in combination with haloperidol. Benevides et al[25] conducted a randomized double-blinded trial on a total of 90, male and female, laparoscopic sleeve gastrectomy (LSG) patients, which aimed to evaluate the efficacy of haloperidol, dexamethasone, and ondansetron in combination therapy to prevent PONV and the need for rescue anti-emetics. Secondary research in this study also involved evaluating the need for analgesics and postoperative IV fluids, hospital length of stay, and incidence of adverse effects.[25] Subjects included in the Benevides et al[25] study were those who had an ASA score of I – III, qualified with a body mass index (BMI) greater than or equal to 35 kg per meter squared (m^2) and were at least 18 years old. Excluded participants were those who received opioids/anti-emetics/hormonal anti-inflammatory medications 24 hours before surgery; experienced serious perioperative complications such as hemorrhage warranting transfusions, cardiac arrest, and shock; struggled with a psychiatric disorder; and reported a migraine history.[25] Other criteria for subject exclusion in the Benevides et al[24] study were contraindication or allergy to ondansetron, haloperidol, or dexamethasone.

Researchers in the Benevides et al[25] study utilized computer-generated randomization lists to allocate subjects to treatment groups; however, did not consider a traditional placebo control group since it was noted that knowingly withholding prophylactic PONV medication would be unethical, especially in surgeries of this nature with a high risk of PONV. Therefore, research conducted by Benevides et al[25] follows a quasi-experimental design since it uses a non-equivalent control group and is classified as good, level II evidence. With the goal of diminishing bias, surgeons, patients, and anesthesiologists were not privy to the allocation of subjects to treatment and comparison control groups.[25] Patients participating in this study were administered 2 mg of IV haloperidol, 8 mg of IV ondansetron, and/or 8 mg of IV dexamethasone based on the groups assigned.[25] The Benevides et al[25] study comparison control group labeled group O that received 8 mg of ondansetron, while treatment groups were the following: group DO was given 8 mg of dexamethasone plus 8 mg of ondansetron, and group HDO received 2 mg of haloperidol with 8 of ondansetron plus 8 mg of dexamethasone. Administration of ondansetron occurred 20 to 30 minutes before surgery was complete, all the while haloperidol and dexamethasone were given after anesthetic induction.[25] All participants who had undergone general anesthesia experienced the following: induction with propofol, fentanyl, cisatracurium, and tracheal intubation; maintenance with a remifentanil infusion, a mixture of inhalation gases: isoflurane, oxygen, and air, and additional cisatracurium as needed; and neuromuscular blockade reversal with neostigmine and atropine.[25] Postoperative feeding consisted of a liquid diet made of a residue-free broth and pain management involved 30 mg of ketolorac plus 20 – 30 mg of dipyrone at induction and every 4 – 8 hours thereafter, in addition to 2 – 3 mg of IV morphine for mild pain experienced in the PACU, and 5 mg of subcutaneous (SC) morphine given prior to transfer out of PACU if pain was moderate to severe.[25] All participants were also eligible for

rescue anti-emetics, 10 mg of IV metoclopramide and/or 30 mg of IV dimenhydrinate, as needed.[25] Throughout the study, researchers collected primary data at different times postoperatively, 24 – 36, 12 – 24, 2 – 12, and 0 – 2 hours, and telephone questionnaires were administered to patients who were discharged prior to 36 hours since surgery.[25] Data analysis involved the use of analysis of variance, Tukey test, Kruskal-Wallis test, Mann-Whitney test, Chi-square/Fischer's exact test, Kaplan-Meier curves, and log-rank test.[25] As a result, statistically significant differences were found among study groups in the Benevides et al[25] study. The HDO group experienced less nausea at 23.7% after 0 – 2 hours and 53.3% after 0 – 36 hours postoperatively compared to group O that experienced nausea 56.7% after 0 – 2 hours and 86.7% after 0 – 36 hours, with a $P = 0.016$ and $P = 0.015$ at each of the time periods, respectively.[25] Researchers also found that there was a statistically significant difference of $P = 0.015$ in the incidence of vomiting at 0 – 36 hours postoperatively between group O with 53.3% and the HDO group with 20%.[25] Just as important, participants in the HDO group were able to wait a longer period of time before administration of a rescue anti-emetic unlike group O that required sooner rescue; this finding was also statistically significant at $P = 0.006$.[25] Throughout the course of the 36-hour observation period, 50% of the HDO group, 40% of the DO group, and 20% of the O group did not exhibit the need for rescue therapy.[25] The Benevides et al[25] trial showed that although hospital length of stay did not change for this surgical population, there was a lower PONV incidence and the use of rescue anti-emetics was reduced in groups that utilized a combined PONV treatment approach including haloperidol, ondansetron, and dexamethasone. Findings by Benevides et al[25] also showed a decreased need for morphine pain management and IV fluids when using this combination therapy. Although some participants commonly reported

dizziness and headache, the adverse effects were minimal and not significantly focused on in this study due to lack of influence on primary results.[25]

Combined Effect of Haloperidol and Dexamethasone on PONV Versus Sole Use of Dexamethasone

In 2015, Joo et al[26] published a randomized, double-blind dose-response and placebo-controlled study that focused on evaluating PONV efficacy with haloperidol in combination with dexamethasone among 150 female patients who had undergone gynecological laparoscopic surgery. Inclusion criteria for subjects considered were ASA score of I – II, age of 20 – 65 years, use of IV PCA, and non-smoking status.[26] The previously delineated inclusion criteria correlates with the presence of 3 Apfel PONV risk factors: non-smoking status, opioid use, and female.[26] Participants were excluded if they met any of the following criteria: hypersensitivity to medications used, BMI greater than 35 kg/m^2, chronic use of a dopamine antagonist, steroid/opioid intake within 7 days of surgery, anti-emetic use 24 hours prior to study, cardiac arrhythmias, kidney/liver/GI/psychiatric disease, diabetes requiring insulin, and inability to utilize a PCA device.[26] Researchers studied subjects who were randomly assigned to two treatment groups; the H1 group received 1 mg of IV haloperidol, the H2 group received 2 mg of IV haloperidol, and the H0 control group received IV saline.[26] Each group had a total of 50 subjects to satisfy an alpha level of 0.05.[26] Therefore, this experimental study qualified as good, level I evidence due to the presence of a traditional control group. Patients, anesthesiologists, and staff evaluating postoperative outcomes were blinded to the allocation of study groups, which was decided by computer-generated codes.[26] The computer-generated codes were placed in opaque envelopes given to a nurse anesthetist not participating in the evaluation of subjects who prepared the medications to be given.[26] This study's blinded design allowed for researchers to

diminish bias as much as possible to prevent compromise of findings. Joo et al[25] participants underwent general anesthesia that involved tracheal intubation and administration of remifentanil, propofol, rocuronium, sevoflurane, air/oxygen, pyridostigmine, and glycopyrrolate. All subjects in the Joo et al[26] study were administered 5 mg of IV dexamethasone during induction, which was received in combination with 1 or 2 mg of IV haloperidol 30 minutes before the end of anesthesia, or alone if solely receiving saline in the control group. At the termination of surgery, participants were administered 1 gram (g) of IV acetaminophen in PACU and started on PCA with 120 mg of ketolorac and 1 mg of fentanyl once discharged from PACU 2 hours later.[26] Data was collected at 2 – 24 hours and 0 – 2 hours postoperatively where the primary focus was on PONV incidence; however, subjects were also evaluated for additional factors such as the need for rescue anti-emetics/analgesics, degree of pain, sedation level, and occurrence of adverse effects of neurological/cardiovascular nature.[26] Data analysis involved one-way analysis of variance (ANOVA), Bonferroni test, Chi-square test, and SPSS version 15.0 for windows.[26] Earlier in the PACU time frame at 0 – 2 hours postoperatively there was no difference observed between groups H2 and H0; however, within 2 – 24 hours postoperatively, subjects in the H1 and H2 group experienced less PONV, 22% and 20% respectively, than the H0 group that scored a higher incidence of PONV at 42%.[26] Results after 24 hours demonstrated that there was a statistically significant difference at $P = 0.003$ in PONV incidence between treatment groups, H1 and H2, and the control group, H0, where 29%, 24%, and 54% of participants experienced PONV respectively.[26] Despite the statistically significant difference between treatment and control groups, researchers found that the incidence of PONV and need for rescue anti-emetics in both treatment groups receiving dissimilar doses of haloperidol was not significantly different.[26] Primary findings from the Joo et al[26] study demonstrated that the 1

mg and 2 mg haloperidol doses were equally effective in preventing PONV when given in conjunction with dexamethasone. According to the Joo et al[26] publication, the combination of dexamethasone with haloperidol was more effective in PONV prevention than dexamethasone as a sole agent. Secondary findings showed that more sedation was observed in the group that received 2 mg dose of haloperidol while other groups showed no significant difference.[26] Three subjects in group H2 also experienced hypotension, which was treated with ephedrine and not of significant influence.[26] All groups did not show a significant difference in pain severity and there were no cardiac or neurologic adverse effects reported.[26]

Chaparro et al[27] also evaluated the efficacy of haloperidol and dexamethasone in PONV prophylaxis among 166 non-smoking women undergoing otorhinolaryngological or cosmetic surgery in 2010. Inclusion criteria were an ASA score of I – II, age 18 – 50 years old, ambulatory plastic/ otorhinolaryngological procedure, and female.[27] Exclusion criteria were a history of EPS, anti-emetic use within 24 hours of surgery, steroid use within 3 months of surgery, or hypersensitivity to morphine, haloperidol, nonsteroidal anti-inflammatory drugs (NSAIDs), or metoclopramide.[27] The Chaparro et al[27] study is considered level II evidence that has a quasi-experimental design since it uses a non-equivalent control group. Participants in the treatment group of the Chaparro et al[27] study were given 1.5 mg of IV haloperidol and 8 mg of IV dexamethasone, which was compared to the placebo group that received 8 mg of IV dexamethasone. All subjects participating were randomly assigned based on a computer-generated list and the hospital pharmacist facilitated the treatment allocation schedule.[27] Besides the hospital pharmacist, all providers involved in patient care were blinded to study groups, which functioned as a method to reduce bias.[27] Throughout the study, additional constants were general anesthetic technique with the administration of midazolam, lidocaine, propofol,

remifentanil infusion, sevoflurane, and rocuronium, as well as analgesia provided by morphine and diclofenac.[27] Blinded evaluators observed patients postoperatively and recorded data at 30 minutes and 2 hours after which a telephone surgery was done at 6 and 24 hours following surgery.[27] Researchers primarily focused on determining the incidence of PONV; however, other factors were also studied such as sedation level, adverse effects, and degree of pain.[27] Data was analyzed using STAT-XACT software in addition to *t*-tests, Mann-Whitney test, and Fisher's exact test.[27] After 30 minutes and 2 hours, researchers did not find any significant difference regarding PONV incidence among study groups and there was no difference regarding sedation level and pain severity.[27] A primary finding showed that there was no statistically significant protective effect for nausea prevention observed with the combination therapy at 6 and 24 hours, but the overall incidence of nausea was lower in the haloperidol with dexamethasone group at 22.5% and 41.5% respectively versus the dexamethasone group at 27.5% and 52.5% respectively.[27] The Chaparro et al[27] publication underscores how the incidence of vomiting was reduced at 6 hours and its decreased incidence became statistically significant at $P < 0.05$ at 24 hours with combination therapy. At 6 hours, patients who received the combination therapy reported a lower incidence of vomiting at 15% versus dexamethasone alone at 26.25%.[27] At 24 hours, patients who received haloperidol and dexamethasone experienced a lower incidence of vomiting at 21.25% versus dexamethasone alone at 41.25%.[27] Therefore, participants who received dexamethasone without haloperidol experienced inferior PONV prophylaxis.[26] Chaparro et al[27] reported no significant adverse effects, including EPS, in patients who received haloperidol.

Combined Effect of Haloperidol and Dexamethasone on PONV Versus Sole Use of Haloperidol, Droperidol, or Dexamethasone

In 2008, Chu et al[28] explored the combined PONV prevention power of haloperidol and dexamethasone among 400 women undergoing laparoscopic-assisted vaginal hysterectomy. Inclusion criteria were women of ASA class I – II scheduled for laparoscopic-assisted vaginal hysterectomy.[28] Exclusion criteria were anti-emetic use within 24 hours of the study, obesity, (BMI greater than 35 kg/m^2), difficult airway, major organ disease, or pregnancy.[28] The Chu et al[28] study is considered an experimental study that has level I evidence due to the randomized assignment of treatment groups and utilization of a traditional control group. Participants in the Chu et al[28] study were divided into the following groups that received: 2 mg of haloperidol with 5 mg of dexamethasone (group H + Dx), 5 mg of dexamethasone (group Dx), 2 mg of haloperidol (group H), 1.25 mg of droperidol (group D), or saline (group S). A computer-generated random number table was used to randomly assign subjects to a treatment or control group.[28] The preparation of medications was performed by a nurse anesthetist who placed all medications in identical syringes containing the medications diluted with saline to total a volume of 2 mL.[28] To reduce bias, all involved in patient care, patients, and investigators collecting postoperative data were blinded to study groups with the exception of the nurse anesthetist preparing medications.[28] All patients were subjected to the same general anesthetic technique with endotracheal intubation and mechanical ventilation that involved the following medications: fentanyl, lidocaine, propofol, rocuronium, desflurane, oxygen, neostigmine, and atropine.[28] Postoperatively, patients were observed for a total of 24 hours during which they were initially observed for 2 hours in the PACU after which they were transferred to a ward.[28] The foci of this experiment centered on determining the severity and incidence of PONV, as well as the need for

rescue anti-emetics.[28] Other factors considered in this study were sedation level, severity of postoperative pain, and the occurrence of treatment side effects such as EPS.[28] Data was analyzed using ANOVA, Bonferroni *t*-test, Kruskal-Wallis test, Mann-Whitney test, Chi-square tests, and Fisher's exact test.[28] After 24 hours, researchers found no significant difference in PONV incidence among groups that received droperidol, haloperidol, or dexamethasone; however, when compared to the saline control group, the groups receiving anti-emetics showed to have a lower incidence of PONV.[28] More specifically, the statistically significant PONV incidences at $P < 0.05$ between 0 – 24 hours were the following in respective groups: 19% with haloperidol plus dexamethasone, 36% with droperidol, 37% with haloperidol, 38% with dexamethasone, and 65% with saline. Additionally, there was no significant difference in the occurrence of EPS, QTc interval changes, sedation, and pain intensity among all groups.[28] The primary finding in this randomized, double-blinded and positive-control study published that patients who received the combination of 2 mg of haloperidol and 5 mg of dexamethasone experienced superior PONV prophylaxis compared to other drugs utilized, which was statistically significant at $P < 0.05$.[28]

Combined Effect of Dexamethasone and Haloperidol or Dexamethasone and Ondansetron on PONV Versus Sole Use of Dexamethasone

In 2012, Wang et al[29] conducted a study on PONV related to PCA on 135 female patients undergoing gynecologic, abdominal, and orthopedic surgeries who were expected to receive morphine PCA. Inclusion criteria for participation in this study were the following: an ASA score of I – II, orthopedic surgery including knee/hip arthroplasty, colorectal abdominal surgery, gynecologic surgery including total/modified hysterectomy, age of 18 – 65 years, and use of morphine PCA.[29] Exclusion criteria involved history of EPS, kidney/hepatic disease, gastric

reflux, cardiac arrhythmia, and difficult intubation.[29] Additionally, patients who had been treated with anti-emetics within 24 hours of surgery were not included in the study.[29] The randomized allocation of subjects to three study groups was facilitated by a computer-generated system; D group received 5 mg of IV dexamethasone, DH group received 2 mg of IM haloperidol 30 minutes within of the end of surgery along with 5 mg of IV dexamethasone at induction, and group DO patients were given 4 mg of IV ondansetron 30 minutes within the end of surgery along with 5 mg of IV dexamethasone at induction.[29] The same general anesthesia technique was performed on all subjects, which involved endotracheal intubation and administration of fentanyl, propofol, rocuronium, sevoflurane, glycopyrrolate, neostigmine, and analgesia provided by morphine PCA pump.[29] Patients who needed rescue anti-emetics received 10 mg of IV metoclopramide and 1 mg of IV ondansetron was given if PONV did not resolve.[29] Researchers aimed to diminish bias by blinding evaluators to the study groups; however, the anesthesiologist was aware of the assignments.[29] Overall, the study demonstrated a quasi-experimental design with good, level II evidence due to the use of a non-equivalent control group and lack of a traditional control group.[29] Data in the Wang et al[28] study was collected over a 24-hour observation period that began 2 hours after surgery and then every 6 hours thereafter.[29] The primary focus of the study aimed to determine the incidence of PONV among different subject groups, but researchers also took into consideration any adverse effects that resulted from each of the medications, as well as sedation level and pain severity.[29] Researchers utilized one-way ANOVA, Bonferroni *t* test, Kruskal-Wallis test, Mann-Whitney ranked-sum test, Chi-square test, Fischer's exact tests to analyze data, which was processed using the 10.0 version of SPSS software compatible with windows.[29] As a result, researchers in the Wang et al[28] study found no significant difference among study groups regarding pain severity, sedation level, or adverse

effects. It is important to note that subjects also did not experience any cardiac arrhythmias throughout the study.[29] When considering the incidence of PONV, subjects in the DO and DH groups showed a significant difference at $P < 0.05$ when compared to group D.[29] Both treatment groups that received haloperidol or ondansetron in combination with dexamethasone experienced diminished PONV incidence and there was less need for rescue anti-emetics over the course of 24 hours.[29] Specifically, total PONV after 24 hours in group D was 25%, which was higher than group DH at 15% and group DO at 13%.[29] Therefore, participants in the Wang et al[29] study showed similar PONV prevention after receiving 5 mg of dexamethasone IV with 2 mg haloperidol intramuscularly (IM) or the combination of 5 mg of dexamethasone IV and 4 mg of ondansetron IV. After administration of 5 mg of dexamethasone IV with 2 mg haloperidol intramuscularly (IM) or the combination of 5 mg of dexamethasone IV and 4 mg of ondansetron IV dosages, there was not an increased incidence of sedation, EPS, or QT prolongation.[29] Findings published by Wang et al[29] also demonstrated that sole treatment of PONV with 5 mg of dexamethasone IV was not as efficacious as combination therapy with haloperidol or ondansetron.

Combined Effect of Haloperidol and Ondansetron on PONV Versus Sole Use of Ondansetron

Grecu et al[30] published a randomized, double-blind trial in 2008 that compared the PONV efficacy between combination therapy and a sole anti-emetic agent among 268 general anesthesia or combined general anesthesia-epidural patients.[30] Inclusion criteria were patients with an ASA class of I – III who were 18 years of age or older that were undergoing general/combined epidural-general anesthesia with a high risk for PONV.[30] Exclusion criteria were patients with history of seizures, Parkinson's disease, cardiac dysrhythmias, prolonged QTc intervals greater than 450 milliseconds (ms), and adverse reactions to ondansetron or haloperidol, as well as those

who have undergone chronic treatment with dexamethasone or dopamine antagonists.[30] The Grecu et al[30] study is considered to have a quasi-experimental design with level II evidence due to the presence of a non-equivalent control group. Participants in the Grucu et al[30] study were randomly divided into two groups that received 1 mg of IV haloperidol and 4 mg of IV ondansetron administered together to evaluate the effect of combination therapy, or 4 mg of IV ondansetron administered alone used for comparison. Intraoperatively, all patients received 4 mg of ondansetron along with the contents of a coded syringe that was randomly assigned 0.2 mL of saline or 1 mg of haloperidol.[30] Per the study, patients and investigators were blinded during the randomization and collection of data process.[30] Patients were observed for PONV in the PACU every 30 minutes until discharged, after which a follow-up phone call was placed 480 minutes after initial PACU admission to further evaluate the patient's postoperative status.[30] Not only was the incidence of PONV studied, but investigators also focused on possible side effects, level of sedation, and need for PONV rescue.[30] Data was analyzed using single factor ANOVA, student's t-test, Kolmogorov–Smirnov test, Wilcoxon's ranked sum test, chi-squared test, Kaplan-Meier survival analysis, log rank test, and STATA 8.0 statistical software.[30] Among patients who received haloperidol and ondansetron the following findings were significant: 90% with complete PONV response after 60 minutes, 76.2% complete PONV response after 480 minutes, 10% with nausea at 60 minutes or less, 23.9% with nausea at 480 minutes or less, 7.7% needing rescue at 180 minutes or less, and 20.8% needing rescue at 480 minutes or less.[30] In comparison, among patients who only received ondansetron, the following findings were significant: 66.2% with complete PONV response after 60 minutes, 59.2% with complete PONV response after 480 minutes, 33.8% with nausea at 60 minutes or less, 42.3% with nausea at 480 minutes or less, 24.1% needing rescue at 180 minutes or less, and 37.6% needing rescue at 480

minutes or less.[30] The time to rescue in those who received haloperidol plus ondansetron was 154.4 ± 133.8 minutes which was longer than ondansetron at 75.3 ± 82.8 minutes.[30] Overall, the combination therapy with haloperidol and ondansetron provided a longer lasting and efficacious PONV prophylaxis versus ondansetron without haloperidol that was statistically significant with a *P* value < 0.001.[30] Additionally, investigators found no significant difference among groups regarding incidence of serious dysrhythmias, QTc prolongation, other toxicity, or sedation.[30] Although there are limitations noted in the Grecu et al[30] study regarding the lack of a standardized surgical population and anesthetic, there are still valid findings found with use of anti-emetics used in combination, which are applicable to PONV prophylaxis in anesthesia practice.[30]

Combined Effect of Haloperidol and Ondansetron on PONV Versus Sole Use of Haloperidol or Ondansetron

In 2009, Feng et al[31] conducted a randomized double-blind study to determine PONV prevention with haloperidol and ondansetron in 210 patients undergoing elective laparoscopic cholecystectomy. Inclusion criteria were patients scheduled for laparoscopic cholecystectomy who were classified as ASA I – II.[31] Exclusion criteria were pregnancy, obesity (BMI > 35 kg/m^2), psychiatric illness, difficult airway, significant major organ disease, anti-emetic drug use within 24 hours of the study, and QTc interval greater than 440 ms.[31] The Feng et al[31] study is considered a quasi-experimental study that has level II evidence due to the randomized assignment of treatment groups and utilization of a non-equivalent control group. A computer-generated random number table was used to randomly assign subjects to a treatment or control group.[31] Participants in the Feng et al[31]study were divided into the following groups that received: 2 mg of IM haloperidol with 2 mL of IV saline (group H), 4 mg of IV ondansetron with

2 mL of IM saline (group O), or 2 mg of IM haloperidol with 4 mg of IV ondansetron (group H + O). IV test drugs were administered after induction and again re-dosed 30 minutes before surgery was complete.[31] Medications were prepared by a nurse anesthetist who labeled syringes IM or IV, and investigators and patients were also blinded during randomization and data collection to reduce bias.[31] General anesthesia with endotracheal intubation and mechanical ventilation was standardized in all patients who received lidocaine, fentanyl, propofol, rocuronium, desflurane, oxygen, neostigmine, and atropine.[31] Postoperatively, patients were observed for a total of 24 hours during which they were initially observed for 2 hours in the PACU after which they were transferred to a ward.[31] The incidence and severity of PONV was primarily studied during this experiment along with the need for rescue anti-emetics.[31] Additionally, the severity of postoperative pain and the occurrence of treatment side effects such as EPS, sedation and prolonged QTc interval, were also studied.[31] Data was analyzed using ANOVA, Tukey's Honestly Significance Difference test, Kruskal-Wallis test, Mann-Whitney test rank sum test, Chi-square tests, and Fisher's exact test.[31] Researchers in the Feng et al[31] study administered 4 mg of IV ondansetron and 2 mg of IM haloperidol versus each drug alone and found that the combination treatment of haloperidol and ondansetron yielded a greater PONV prevention response and an increase in patient satisfaction. The total PONV incidence among patients who received haloperidol plus ondansetron was 21% at 0 – 24 hours; however, there was 39% at 0 – 24 hours for those who only received haloperidol and 38% at 0 – 24 hours for those who only received ondansetron.[31] Just as important, the complete PONV response was 79% in the group that received haloperidol plus ondansetron; yet, 62% and 61% in subjects who received ondansetron and haloperidol respectively.[31] Patients who received haloperidol plus ondansetron had a higher satisfaction score of 8.3 ± 1.8 when compared to ondansetron with 7.2

± 2.5 and haloperidol with 7.0 ± 2.4.[31] After 24 hours, there was no significant difference in the incidence of PONV and need for rescue analgesics among groups that only received haloperidol or ondansetron ($P < 0.05$).[31] There was also no significant difference in QTc prolongation, incidence of EPS, and sedation level among all groups.[31] Of significant importance was that subjects who received both haloperidol and ondansetron suffered the lowest incidence of PONV and required less rescue analgesics or anti-emetics.[31] Thus, findings in the Feng et al[31] study point to a statistically significant superior PONV prophylaxis with combination therapy involving haloperidol plus ondansetron at $P < 0.05$.

Summary of the Evidence

The most current research centers around adult surgical patients undergoing general anesthesia who have received PONV prophylactic treatment. The literature mainly points to documenting the incidence of PONV during the perioperative period despite anti-emetic treatment in laparoscopic hysterectomy, laparoscopic cholecystectomy, laparoscopic sleeve gastrectomy, laparoscopic gynecological, orthopedic, abdominal, cosmetic, and otorhinolaryngological surgery patients. All articles discussed haloperidol administration in combination PONV treatment except for Dağ et al[32] that studied haloperidol's efficacy as a sole agent. The anti-emetics used with haloperidol varied slightly; one study, Benevides et al,[25] administered haloperidol with dexamethasone and ondansetron, while four studies analyzed the efficacy of haloperidol with dexamethasone and two studies focused on the efficacy of haloperidol with ondansetron.

The selected publications that studied PONV prophylaxis with haloperidol focused on the PONV incidence with opioid analgesia administered in two different ways. Two research groups, Dağ et al[32] and Wang et al[29] utilized PCA opioid analgesia postoperatively, while five studies

Benevides et al,[25] Joo et al,[26] Chaparro et al,[27] Chu et al,[28] Feng et al[31] aimed for narcotic pain management administered by anesthesia providers avoiding PCA. All study subjects only received fentanyl during induction to facilitate tracheal intubation except for those in the Joo et al[26] and Chaparro et al[27] studies who received a remifentanil infusion and Benevides et al[25] subjects who received both fentanyl for induction and a remifentanil infusion during maintenance. One study, Grecu et al,[30] did not specify the type or method of narcotic used during general anesthesia. All studies except for three, Benevides et al,[25] Grecu et al,[30] and Feng et al[31] used females as subjects, which provided a representation of the overall population.

In general, all studies showed a decreased incidence of postoperative vomiting when haloperidol was administered in combination with other anti-emetics, dexamethasone and ondansetron, or haloperidol used alone. More than 85% of literature selected showed that haloperidol provided a protective effect against postoperative nausea when used in combination treatment and as a sole agent. Additionally, all subjects receiving haloperidol for PONV prophylaxis, in combination therapy or alone, did not exhibit significant adverse effects, increased sedation level, or a greater pain medication requirement.

Conclusion

Research demonstrates that PONV negatively affects surgical patients despite the use of available anti-emetic treatments. According to the algorithm published by the British Journal of Anesthesia and the guidelines suggested by the International Anesthesia Research Society, which is supported by the ASA and AANA, combination PONV prophylaxis is modeled as a goal of perioperative care.[8-9] Within the International Anesthesia Research Society's guidelines, haloperidol is featured as a prophylactic anti-emetic that showcases its reasonable capacity for inclusion in anesthesia practice.[8]

Rationale

Although the literature presented is valid and significant, diminished adherence to combination PONV prophylaxis recommendations, especially with haloperidol, has been noted as an issue in current practice.[8-9] This dissemination brings to light the promising potential of haloperidol in different surgical settings and various treatment types, which can be appealing for anesthesia providers who share the goal of optimal PONV prophylaxis. If the presentation of this inclusive research positively influences anesthesia provider attitudes and increases knowledge respectively, there is the possibility for its application in current anesthesia practice to diminish the incidence of PONV as evidenced by the analyzed literature.

Objectives

DNP Project Goals

PONV is considered a common postoperative adverse event that warrants prevention.[8-9] Although different anti-emetics have been utilized in practice with effects on various PONV associated receptors, patients continue to suffer from poor outcomes.[8-9] Negative outcomes reported include delayed hospital discharge, poor patient satisfaction, increased costs, and complications such as aspiration, airway compromise, electrolyte disturbances, bleeding, dehydration, wound dehiscence, ruptured esophagus, and limited oral intake.[1,5,11,14] According to the International Anesthesia Research Society and the British Journal of Anesthesia, current recommendations point to the use of combination medication therapy for PONV prophylaxis, which shows significant promise in diminishing the debilitating outcomes associated with poor PONV prevention compared to the use of anti-emetics as sole agents.[8-9]

Among the research gathered and reviewed, haloperidol has been showcased as an efficacious PONV prophylactic medication; however, its use is not consistent despite the

suggestion of butyrophenones in current algorithms.[9] It is hypothesized that the decreased use of haloperidol can be attributed to a lack of knowledge regarding its value.[9] The primary goal of improving anesthesia provider knowledge and attitude is to show the benefit of incorporating haloperidol in adult PONV prophylaxis to complement the guidelines proposed by the International Anesthesia Research Society. The objective of this Quality Improvement Project is to improve anesthesia provider knowledge and attitudes regarding haloperidol's efficacy in preventing PONV which can set the foundation for the application of evidence-based practice for PONV prophylaxis.

SMART Goals and Outcomes

In efforts to formulate goal objectives, the SMART framework was implemented. The SMART framework entails utilizing objectives that are specific, measurable, achievable, realistic, and timely.[33]

Specific

Anesthesia providers will have an education module on the utilization of haloperidol as a pharmacological complement for PONV prophylaxis in adult surgical patients.

Measurable

The value of the educational module will be gauged through pre and post questionnaires that assess anesthesia provider knowledge and attitudes prior to participation and after the PowerPoint educational module. Measurement of outcomes will be realized before and after intervention taking into consideration the variation in anesthesia provider feedback in respect to knowledge of the use of haloperidol as an anti-emetic, combination PONV therapy, and PONV. Qualtrics will provide the software to streamline surveys and facilitate a compilation of data with respective analysis.

Achievable

Certified Registered Nurse Anesthetists (CRNAs), Anesthesiologists, and Anesthesia Assistants (AAs) in affiliated hospital systems will provide a sufficient sample size to generate findings indicating whether learning has occurred in respect to the PONV prophylaxis potential of haloperidol, especially in combination therapy. Additionally, findings will also provide insight into whether anesthesia provider attitudes towards haloperidol use in practice reflect a positive or negative outlook.

Realistic

Anesthesia providers will be educated on the suggested utilization of haloperidol for PONV prophylaxis in adult surgical patients along with commonly administered anti-emetics used in combination. Multi-media presentation will provide the primary avenue of highlighting a PONV algorithm.

Timely

Over the course of eight months, the primary investigator will collect data, analyze findings, and disseminate statistically significant results. Anesthesia providers will be allotted a four-week time-period to participate in the QI project. Pertinent outcomes of this QI project will showcase the quality of the educational module taught that focuses on the efficacy of haloperidol as a pharmacological complement in PONV prophylaxis, and the receptivity of CRNAs, AAs, and anesthesiologists to apply findings in practice that are centered around utilizing combination therapy.

Program Structure

The success of this educational module in improving knowledge and attitudes among anesthesia providers depends on the support of all stakeholders. Vital stakeholders are identified

as participants and care providers who aim to facilitate a practice change that involves promoting the use of haloperidol as a pharmacological complement in PONV prophylaxis. The aforesaid is realized through mobilizing the anesthesia community to influence perioperative practice, which parallels appreciating the associated positive outcomes of haloperidol use in PONV prophylaxis. Through a pre-intervention questionnaire, participants' baseline knowledge and attitudes can be assessed regarding PONV, haloperidol's role in PONV prophylaxis, PONV management, and the negative outcomes associated with PONV. An educational module provided to anesthesia providers will model the benefits of haloperidol use in PONV prophylaxis and highlight the role of its medication class in currently recommended PONV guidelines. The presentation of this educational module and surveying of participants can be facilitated by hospital system electronic mail and inclusion of in-services per approval of hospital institutional review board regulations. Following the exhibition of the educational module, participants will complete a post survey to evaluate learning. A strengths, weaknesses, opportunities, and threats (SWOT) analysis is instrumental in understanding the essential variables that influence and guide the development of this QI project.[34] In comprehending and addressing the SWOT analysis variables, buttressing weaknesses can initiate project strengths and detection of threats can birth opportunities.[34]

SWOT Analysis

Strengths and Opportunities

According to Helms and Nixon,[34] opportunities coincide strongly with the strengths of any venture that involves strategic management. Strengths in a SWOT analysis delineate what factors are present that promote the appreciation of opportunities.[34] Implementation of PONV prophylaxis algorithms in anesthesia practice encourage the use of combination anti-emetic therapy, which has been tied to improved postoperative patient outcomes highlighting a crucial

strength.[8-9] It is anticipated that incorporation of haloperidol in current PONV practice can enhance the recovery process of patients underscoring a pivotal opportunity.[20,25-32] The collaboration of motivated anesthesia providers inspired to transform the postoperative experience can begin with access to learning the opportunities present to induce an evolution of perioperative practice patterns.[35] To make this possible, recruitment of anesthesia providers to participate and endorse the paradigm shift to diminish PONV is necessary. While anesthesia providers are the primary stakeholders in this QI project, the aspired outcome of improving knowledge and attitudes of PONV provides additional opportunities for the involvement of supplemental stakeholders such as patients and post anesthesia care unit (PACU) nursing staff.[35] Through the dissemination and publication of this QI project's findings, there is room for an increased demand for patient-centered care that includes patient shared decision-making, as well as the participation of medical staff essential in the care and recovery of adult surgical patients.[35-36] The aforesaid factors reinforce the potential success of this QI project and may promote the coexisting goal of compliance and practice change among anesthesia providers that considers haloperidol use for PONV combination therapy.[35]

Weaknesses and Threats

Helms and Nixon[34] also identify that any program's weaknesses can delay progress and amplify threats. Unfavorable internal and external issues can underscore weaknesses and act as project failure catalysts that can hinder overcoming the risk of a persistent threat to project implementation.[34] Anesthesia providers' dearth of knowledge regarding the studied topic can be a primary weakness in promoting practice change.[35] Failure to adhere to guidelines suggested for PONV prophylaxis can also pose as a threat to long-term compliance in practice and propagation of available PONV knowledge.[9] Additionally, variations in anesthesia provider training, beliefs

about medication efficacy/side-effects, and judgement can be classified as threats.[37] Therefore, anesthesia provider bias regarding PONV prophylaxis can be detrimental and threatens the development of this QI project.

Organizational Factors

The implementation of a PONV prophylaxis education module that highlights the value of haloperidol in combination PONV therapy serves as an opportunity to combat threats to perioperative practice change and QI project development. Utilization of diagrams that correlate with the applicable literature facilitate a visual depiction of the suggested PONV algorithm that includes haloperidol. Sufficient sponsorship with an anesthesia team that shares the same objective as the surveyor is critical for the support of this PONV educational module. The participating anesthesia team can provide a reservoir of information critical to evaluating the efficacy of the educational module presented. Data analysis can provide a report of knowledge deficit present and highlight learning that occurred among participating anesthesia providers. Understanding data, studying how findings align with QI project goals, and providing a corresponding dissemination are vital to evaluating the educational module. Dissemination components include background information, PICO question, methods, results, data analysis process, conclusions, limitations, and opportunities for improvement.

Conceptual Underpinning and Theoretical Framework

A theoretical framework integrated into research provides a structure that guides the study and highlights a rationale for suggested practice.[38] The middle-range nursing theory that will be used to guide the development of this QI project is the Theory of Unpleasant Symptoms (TOUS).[38-39] While patients commonly suffer from PONV, there are other postoperative outcomes that can occur simultaneously, such as pain, bleeding, venous hypertension,

esophageal rupture, wound dehiscence, decreased oral intake, electrolyte disturbances, dehydration, and airway compromise.[1,5,11,14] The TOUS allows for the consideration of multiple symptoms that can interact with each other and affect patient outcomes postoperatively; this provides a realistic representation of the perioperative process.[38-39] This theory models how symptoms can act synergistically when presenting together and how control of one symptom can assist with the management of others.[38] In providing anesthesia providers with updated valuable knowledge through the implementation of a PONV educational module, the management of the unpleasant symptoms of PONV can be further understood.[39] By employing suggested evidence-based practice promoted in the PONV educational module, there is the potential for anesthesia providers to diminish the incidence of PONV with the use of haloperidol and combination anti-emetic therapy.[39] In application of the TOUS, it is hypothesized that addressing PONV may assist with management of other postoperative symptoms that afflict patients.[38]

Methodology

Setting and Participants

This DNP project will take place at Memorial Regional Hospital located in Hollywood, Florida. The primary project participants will be the anesthesia providers. The participants will be recruited voluntarily via email and the anticipated sample size will be between 4 – 10 participants.

Description of Approach and Project Procedures

The primary methodology of the proposed project is to administer an online educational module to anesthesia providers that focuses on the significance of PONV in anesthesia practice and the impact of combination PONV prophylaxis utilizing haloperidol. All phases of the educational module can be completed with the use of a computer, tablet, or smartphone. The

project will be implemented in the first phase by conducting an online pre-test that will gauge baseline knowledge and attitudes on the subject. The second phase will be comprised of a PowerPoint presentation as the primary means of learning that includes important information regarding PONV, PONV prophylaxis, and the role of haloperidol and other anti-emetic agents in anesthesia practice. The third phase of the project will involve a post-test to evaluate knowledge gained and any changes in anesthesia provider attitudes about the subject presented. The results will provide feedback regarding the impact of the educational intervention and how the proposed PONV prophylaxis clinical recommendations influence anesthesia provider attitudes.

Protection of Human Subjects

Initial project approval by the Institutional Review Board (IRB) of Florida International University (FIU) is a prerequisite for the launch of the educational module. For this QI project, the recruitment population will include anesthesia providers who work at Memorial Regional Hospital and are involved in anesthesia practice. Recruitment activities will be conducted via email with the invitation indicating voluntary participation without penalty for withdrawing from the QI project. Participating anesthesia providers will benefit from an increase in knowledge and improvement in attitude about utilizing haloperidol as a pharmacological complement for PONV prophylaxis in adult surgical patients. The main risks for this quality improvement project are minimal. As with any educational module, potential minimal risks are mild emotional stress or physical discomfort from sitting on a chair for an extended period of time.

Data Collection

In this project, the primary tools that will be utilized to evaluate the effectiveness of the intervention are a pre-test and post-test that follow a survey format. Qualtrics will be used to implement both 16-question surveys that inquire about knowledge of PONV, haloperidol, and

PONV prophylaxis using combination therapy. Participants will also be asked to express attitudes regarding the inclination to implement haloperidol into anesthesia practice and the administration of haloperidol as a complementary drug to decrease PONV. Other collected data include the following: participant gender, age, ethnicity, level of education, and years of experience. The pre-test survey will provide an evaluation of baseline knowledge on the subject and identify any knowledge gaps that would warrant the implementation of the educational module. The post-test survey will reveal if participants learned from the educational module and are willing to incorporate what was learned into anesthesia practice. The data collected will be confidential and no subject identifiers will be recorded during any component of the QI project.

Data Management and Analysis Plan

The primary investigator for the project will be the DNP student who will be implementing the surveys. All data collected will be stored in a password protected database accessible by the primary investigator and DNP project supervisor. There will be no record of participant personal identifiers to protect confidentiality. The efficacy of the intervention will be measured by comparing the pre-test answers to those of the post-test with the assistance of statistical analysis.

Results

Pre-Test Demographics

The pre-test demographics are displayed in Table 1, shown below.

Table 1. ***Pre-Test Participant Demographics***

Demographic	**n (%)**
Total Participants	6 (100.00%)
Age	

25-34	3 (50.00%)
35-44	0 (0.00%)
45-54	3 (50.00%)
55-64	0 (0.00%)
65+	0 (0.00%)
Gender	
Male	2 (33.33%)
Female	4 (66.67%)
Ethnicity	
African American	1 (16.67%)
Caucasian	2 (33.33%)
Hispanic	2 (33.33%)
Other	1 (16.67%)
Medical Profession	
CRNA	6 (100.00%)
AA	0 (0.00%)
Anesthesiologist	0 (0.00%)
Other	0 (0.00%)
Highest Education	
Associate's degree	0 (0.00%)
Bachelor's degree	0 (0.00%)
Master's degree	0 (0.00%)
Doctoral degree	6 (100.00%)
Experience	
Less than 1 year	2 (33.33%)
1 to 5 years	1 (16.67%)
6 to 10 years	0 (0.00%)
More than 10 years	3 (50.00%)

There were six participants in the pre-test demographics, and all completed the pre-test survey. Most of the participants were female (n=4, 66.67%), as opposed to male (n=2, 33.33%). There were also a range of ethnicities represented: African American (n=1, 16.67%), Caucasian (n=2, 33.33%), Hispanic (n=2, 33.33%), and other (n=1, 16.67%). Information was obtained regarding the participant's role at the hospital, and it was found that all participants were

Certified Registered Nurse Anesthetists (CRNAs) (n=6, 100%). The participants were questioned about the length of time practicing, finding that the practice period ranged: less than one year (n=2, 33.33%), 1 to 5 years (n=1, 16.67%), 6 to 10 years (n=0, 0%), and more than 10 years (n=3, 50.00%).

Pre-Test PONV Knowledge

Pre-test knowledge on PONV showed that two participants (33.33%) were aware that the incidence of PONV can be as high as 80%. Therefore, a majority of participants (66.67%) were unaware of the clinical incidence of PONV. When asked to select the unpleasant symptoms associated with PONV contributing to considerable patient morbidity and distress, three participants (50.00%) selected the correct answer that included esophageal rupture, wound dehiscence, aspiration, and dehydration.

Pre-Test Haloperidol PONV Prophylaxis Knowledge

Before the educational intervention, half of the participants (n=3, 50.0%) knew that the most efficacious parenteral dose range of haloperidol for PONV prophylaxis is 0.5 – 2 mg. Most participants (n=4, 66.67%) knew that haloperidol is classified as a dopamine D2 receptor antagonist. When asked to select all of haloperidol's mechanisms of action that contribute to its clinical effects, the correct answer was selected once (12.5%), and seven of the eight answers chosen were incorrect (87.5%). Three participants (50.00%) knew what population of surgical patients would benefit from PONV prophylaxis with haloperidol, which are patients undergoing otorhinolaryngological, ophthalmic, laparoscopic, and gynecological procedures. When asked to select all of the disease processes (Parkinson's disease, neuroleptic malignant syndrome, acute/chronic dysrhythmias, and QT prolongation) that should preclude the use of haloperidol, the correct answer was selected three times (42.86%) and four of the seven answers chosen were

incorrect (57.14%). When asked to select two potential side effects of haloperidol at high doses, such as 35 mg or more, the majority of answers chosen (n=9, 75%) were correct. When asked to identify what two other medications have shown superior PONV prophylaxis when used in combination with haloperidol, most answers (n=7, 58.33%) selected were correct and identified dexamethasone and ondansetron. Only one participant (16.67%) knew that PONV prophylaxis is most efficacious when haloperidol is administered at any time intraoperatively. Half of the participants (50.00%) knew that haloperidol's onset of action for PONV prophylaxis is 30 minutes, two participants (33.33%) knew that haloperidol's duration of action for PONV prophylaxis is 4 hours, and one participant (16.67%) knew that haloperidol's elimination half-life is 12 – 35 hours.

Pre-Test Utilization and Attitudes of Haloperidol PONV Prophylaxis

The inclination to implement haloperidol into anesthesia practice prior to the educational module was low. Three participants (50.00%) were unsure, and one participant (16.67%) was very unlikely to use haloperidol. Only two participants (33.33%) were likely to use haloperidol in anesthesia practice. When asked how likely they were to administer haloperidol in combination therapy for PONV prophylaxis, two participants (33.33%) were somewhat likely, while two participants (33.33%) were somewhat unlikely, and two participants (33.33%) were most unlikely. Therefore, a majority of participants (n=4, 66.66%) were unlikely to use haloperidol in combination therapy for PONV prophylaxis. Attitudes toward the administration of haloperidol as a complementary drug to decrease PONV were divided: one participant

(16.67%) was very positive, two participants (33.33%) were positive, two participants (33.33%) were neutral, and one participant (16.67%) was very negative.

Post-Test Demographics

Table 2 (see below) shows the post-test demographics.

Table 2. ***Post-Test Participant Demographics***

Demographic	**n (%)**
Total Participants	5 (100.00%)
Age	
25-34	3 (60.00%)
35-44	0 (0.00%)
45-54	2 (40.00%)
55-64	0 (0.00%)
65+	0 (0.00%)
Gender	
Male	1 (20.00%)
Female	4 (80.00%)
Ethnicity	
African American	1 (20.00%)
Caucasian	2 (40.00%)
Hispanic	1 (20.00%)
Other	1 (20.00%)
Medical Profession	
CRNA	5 (100.00%)
AA	0 (0.00%)
Anesthesiologist	0 (0.00%)
Other	0 (0.00%)
Highest Education	
Associate's degree	0 (0.00%)
Bachelor's degree	0 (0.00%)
Master's degree	0 (0.00%)
Doctoral degree	5 (100.00%)
Experience	

Less than 1 year	2 (40.00%)
1 to 5 years	1 (20.00%)
6 to 10 years	0 (0.00%)
More than 10 years	2 (40.00%)

There were five participants in the post-test demographics, and all completed the survey. Most of the participants were female (n=4, 80.00%), as opposed to male (n=1, 20.00%). There were also a range of ethnicities represented: African American (n=1, 20.00%), Caucasian (n=2, 40.00%), Hispanic (n=1, 20.00%), and other (n=1, 20.00%). Information was obtained regarding the participant's role at the hospital, and it was found that all participants were Certified Registered Nurse Anesthetists (CRNAs) (n=5, 100%). The participants were questioned about the length of time practicing, finding that the practice period ranged: less than one year (n=2, 40.00%), 1 to 5 years (n=1, 20.00%), 6 to 10 years (n=0, 0%), and more than 10 years (n=2, 40.00%). It is noted that while there were fewer people completing the post-test survey, the distribution of the sample was similar across both pre- and post-tests.

Post-Test PONV Knowledge

After the educational module, anesthesia provider knowledge on PONV improved. A majority of participants (n=3, 60.00%) were aware that the incidence of PONV can be as high as 80%. Therefore, a minority of participants (n=2, 40.00%) were unaware of the clinical incidence of PONV. When asked to select the unpleasant symptoms associated with PONV contributing to considerable patient morbidity and distress, the correct answer that included esophageal rupture, wound dehiscence, aspiration, and dehydration was selected by four participants (66.67%), while incorrect answers were chosen by one participant (33.33%). There was a PONV knowledge improvement noted for all questions. Table 3 shows the differences in responses from the pre- to post-test.

Table 3. ***PONV Knowledge Pre- and Post-Test***

Question	Correct in Pre-test	Correct in Post-test	Difference
The incidence of postoperative nausea and vomiting can be as high as:	33.33%	60.00%	26.67%
What are unpleasant symptoms associated with PONV contributing to considerable patient morbidity and distress? (Select all that apply)	50.00%	66.67%	16.67%

Post-Test Haloperidol PONV Prophylaxis Knowledge

Anesthesia provider knowledge on haloperidol for PONV prophylaxis improved overall after the educational module. All participants (n=5, 100.0%) knew that the most efficacious parenteral dose range of haloperidol for PONV prophylaxis is 0.5 – 2 mg. Most participants (n=3, 60.00%) knew that haloperidol is classified as a dopamine D2 receptor antagonist. When asked to select all of haloperidol's mechanisms of action that contribute to its clinical effects, the correct answer was selected three times (42.86%) and four of the seven answers chosen were incorrect (57.16%). When asked what population of surgical patients would benefit from PONV prophylaxis with haloperidol, the correct answer was chosen three times (42.86%) and four of the seven answers chosen were incorrect (57.16%). When asked to select all of the disease processes that should preclude the use of haloperidol, the correct answer was selected three times (42.86%) and four of the seven answer combinations chosen were incorrect (57.16%). When asked to select two potential side effects of haloperidol at high doses, such as 35 mg or more, the majority of answers (n=8, 80%) were correct. When asked to identify what two other medications have shown superior PONV prophylaxis when used in combination with

haloperidol, most answers (n=8, 80.00%) selected were correct and identified dexamethasone and ondansetron. Two participants (40.00%) knew that PONV prophylaxis is most efficacious when haloperidol is administered at any time intraoperatively. Four participants (80.00%) knew that haloperidol's onset of action for PONV prophylaxis is 30 minutes, four participants (80.00%) knew that haloperidol's duration of action for PONV prophylaxis is 4 hours, and three participants (60.00%) knew that haloperidol's elimination half-life is 12 – 35 hours. There was a knowledge improvement noted in a majority of questions regarding haloperidol for PONV prophylaxis. Table 4 shows the differences in responses from the pre- to post-test.

Table 4. ***Haloperidol PONV Prophylaxis Knowledge Pre- and Post-Test***

Question	Correct in Pre-test	Correct in Post-test	Difference
What is the most efficacious parenteral dose of haloperidol for PONV prophylaxis according to most recent literature?	50.00%	100.00%	50.00%
What classification of anti-emetic is haloperidol considered?	66.67%	60.00%	- 6.67%
Haloperidol's clinical effects can be attributed to what mechanism(s) of action? (Select all that apply)	12.5%	42.86%	30.36%
What population of surgical patients can benefit from PONV prophylaxis with haloperidol? (Select all that apply)	50.00%	42.86%	- 7.14
Haloperidol should be excluded from patients presenting with which disease process(es) or conditions? (Select all that apply)	42.86%	42.86%	0.00%
Potential side effects of haloperidol at high doses, such as 35 mg or more, include (Select 2)	75.00%	80.00%	5.00%

Utilization of haloperidol in combination with what other medications have shown superior PONV prophylaxis? (Select 2)	58.33%	80.00%	21.67%
PONV prophylaxis is most efficacious when haloperidol is administered when intraoperatively?	16.67%	40.00%	23.33%
What is haloperidol's onset of action for PONV prophylaxis?	50.00%	80.00%	30.00%
What is haloperidol's duration of action for PONV prophylaxis?	33.33%	80.00%	46.67%
What is haloperidol's elimination half-life?	16.67%	60.00%	43.33%

Post-Test Utilization and Attitudes of Haloperidol PONV Prophylaxis

The inclination to implement haloperidol into anesthesia practice was high after the educational module intervention. One participant (20.00%) was very likely, and four participants (80.00%) were likely to implement haloperidol into anesthesia practice. When asked how likely they were to administer haloperidol in combination therapy for PONV prophylaxis, one participant (20.00%) was most likely, while four participants (80.00%) were somewhat likely. Therefore, all participants (n=5, 100.00%) were more inclined to use haloperidol in combination therapy for PONV prophylaxis and in anesthesia practice after the educational module. Attitudes toward the administration of haloperidol as a complementary drug to decrease PONV were improved: two participants (40.00%) were very positive, one participant (20.00%) was positive, and two participants (40.00%) were neutral. There were no negative or very negative attitudes expressed regarding haloperidol use in complementary PONV prophylaxis after the educational module. Table 5 shows the differences in responses from the pre- to post-test.

Table 5. ***Utilization and Attitudes of Haloperidol PONV Prophylaxis Pre- and Post-Test***

Question	Pre-test	Post-test	Difference
How likely are you to implement haloperidol into your anesthesia practice?			
Very likely	0.00%	20.00%	20.00%
Likely	33.33%	80.00%	46.67%
Unsure	50.00%	0.00%	- 50.00%
Unlikely	0.00%	0.00%	0.00%
Very unlikely	16.67%	0.00%	- 16.67%
How likely are you to administer haloperidol in combination therapy for PONV prophylaxis?			
Most likely	0.00%	20.00%	20.00%
Somewhat likely	33.33%	80.00%	46.67%
Somewhat unlikely	33.33%	0.00%	-33.33%
Most unlikely	33.33%	0.00%	-33.33%
What is your attitude toward the administration of haloperidol as a complementary drug to decrease PONV?			
Very positive	16.67%	40.00%	23.33%
Positive	33.33%	20.00%	- 13.33%
Neutral	33.33%	40.00%	6.67%
Negative	0.00%	0.00%	0.00%
Very negative	16.67%	0.00%	- 16.67%

Discussion

Limitations

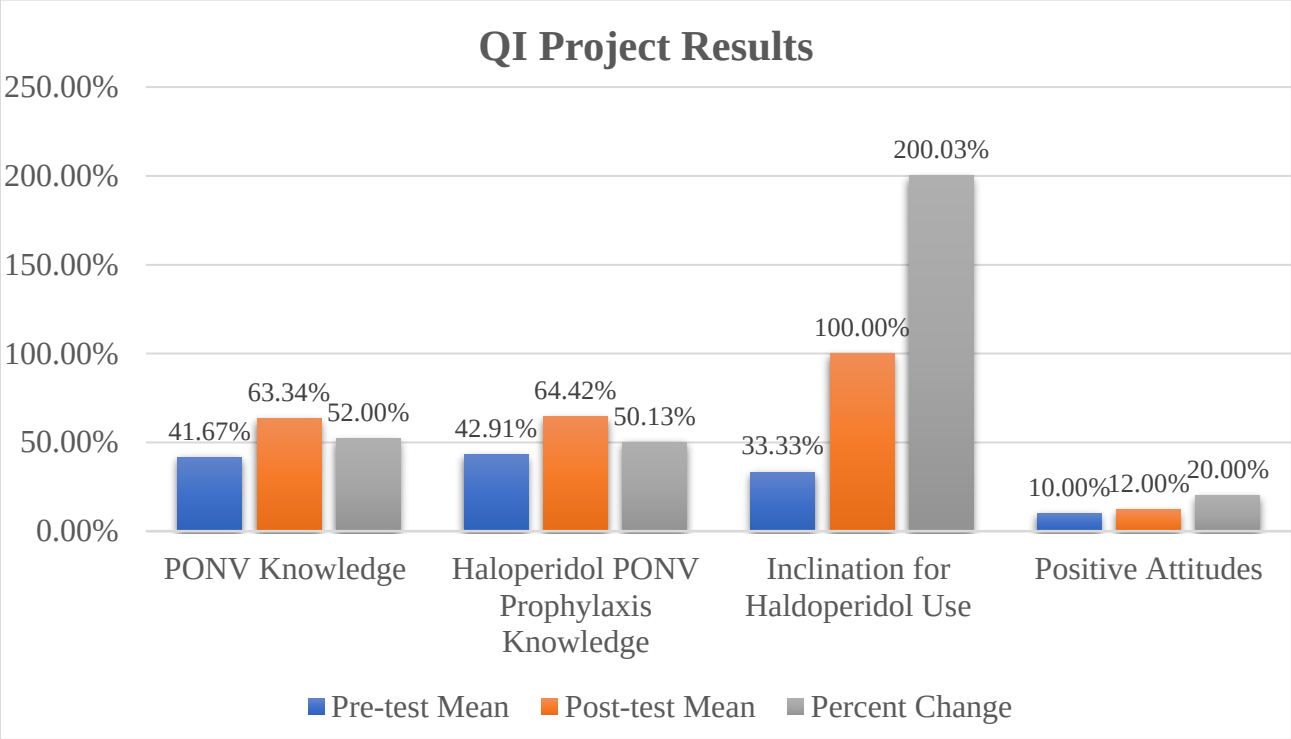
In this QI project, there were limitations noted, small sample size was a limitation despite the large number of potential participants invited to participate. Although there were thirty-seven anesthesia providers from Memorial Regional Hospital invited to participate, six CRNAs completed the pre-test, and only five CRNAs completed the post-test. After the educational module was launched, anesthesia providers were reminded once via email to participate, and the window to participate was one month long. The online modality of the educational module also

contributed to this QI project's limitations since the project was asynchronous and completed entirely online. While the educational module delivery method posed as a barrier to presenting the material to more providers, this QI project would have benefited from a live presentation format in efforts to improve recruitment. Another limitation of this QI project was the inclusion of one hospital facility. Potential factors to mitigate limitations are to address issues with recruitment, allow for expansion of participation to other sites, and extend the time period to participate.

Summary

The results show that there was a statistical difference between the pre-and post-tests. The average amount of correct answers in the PONV knowledge pre-test were 41.67%, and an average of 63.34% correct answers were noted in the post-test. The average amount of correct answers in the haloperidol PONV prophylaxis knowledge pre-test was 42.91%, and an average of 64.42% correct answers were reflected in the post-test. Therefore, a significant improvement in knowledge regarding PONV and haloperidol PONV prophylaxis was observed in all respondents with a 52.00% percent change and 50.13% percent change identified respectively. The average amount of anesthesia providers inclined to utilize haloperidol in anesthesia practice and for PONV prophylaxis were 33.33% in the pre-test, and 100.00% in the post-test. Overall, there was an increase in the inclination to utilize haloperidol in anesthesia practice and for PONV prophylaxis with a 200.03% percent change observed. The mean number of positive answers observed in the pre-test surveying attitudes regarding haloperidol use for PONV prophylaxis were 10.00%, and 12.00% in the post-test. There was also a significant improvement in attitudes observed in all respondents regarding haloperidol use for PONV prophylaxis with a 20.00% percent change. The following figure demonstrates the aforementioned findings.

Figure 7. ***QI Project Results***



Future Implications for Advanced Nursing Practice

The implementation of the educational module can function as a segue in anesthesia practice change. By showcasing literature on PONV and haloperidol PONV prophylaxis, the information available to anesthesia providers can influence the inclination to use haloperidol in anesthesia practice and as a complement drug with other anti-emetics for PONV prophylaxis. The impact of the intervention is vital because it's educational efficacy and ability to influence the attitudes of anesthesia providers regarding haloperidol use, can affect adult surgical patient outcomes. The data showed that the QI project was successful in increasing anesthesia providers' knowledge and attitudes. The findings appreciated in this QI project can trigger further research considering haloperidol and PONV prophylaxis. Despite the value of current literature, there is a need for further research on haloperidol's role in other clinical settings, such as when implementing an anesthesia plan that involves multimodal analgesia.

Conclusions

The results of this QI project offered valuable insight about how anesthesia provider knowledge and attitudes are affected by an educational module considering haloperidol in combination PONV prophylaxis. The findings assumed a positive relationship; anesthesia provider knowledge on haloperidol and PONV prophylaxis increased, inclination to utilize haloperidol in practice and for PONV prophylaxis increased, and overall attitudes improved. Ultimately, this QI project was able to respond to the following research question: (P) In adult surgical patients (I) does an educational module on the utilization of haloperidol as a pharmacological complement for PONV prophylaxis (C) versus no educational module (O) increase anesthesia provider knowledge and attitude in implementing haloperidol as an adjunct treatment in the management of PONV?

Appendix

Appendix A: Summary of the Literature Table

Author(s)	Purpose	Methodology / Research Design	Intervention(s)/ Measures	Sampling/Setting	Primary Results	Relevant Conclusions
Benevides et al,[25] **(2013)**	To investigate and compare the PONV prophylaxis efficacy of anti - emetics used in combination and as sole agents.	Randomized double-blinded study. Quasi-experimental Level II	Randomized double-blinded study conducted evaluating PONV prophylaxis using the combination of haloperidol, ondansetron, and dexamethasone compared to the sole use of ondansetron or dexamethasone with ondansetron.[24]	Male and female patients at least 18 years old undergoing general anesthesia for laparoscopic sleeve gastrectomy with an ASA classification of I – III and BMI $\geq$ 35 kg/m^2.[24] Sample size n= 90	Patients who received haloperidol, dexamethasone, and ondansetron experienced less nausea at 23.7% after 0 – 2 hours and 53.3% after 0 – 36 hours postoperatively compared to patients who only received ondansetron and experienced nausea 56.7% after 0 – 2 hours and 86.7% after 0 – 36 hours, with a $P = 0.016$ and $P = 0.015$ at each of the time periods, respectively.[24] There was a statistically significant difference of $P = 0.015$ in the incidence of vomiting at 0 – 36 hours postoperatively between the ondansetron group with 53.3% and the haloperidol, dexamethasone, ondansetron group with 20%[24]	Lower PONV incidence and the use of rescue anti-emetics was reduced in groups that utilized a combined PONV treatment approach including haloperidol, ondansetron, and dexamethasone.[24]

Joo et al,[26] **(2015)**	To investigate haloperidol's efficacy in PONV prophylaxis as an agent in combination therapy and identify haloperidol's most efficacious dose.[25]	Randomized double-blinded dose response and placebo-controlled study. Experimental study Level I	Randomized double-blinded study conducted evaluating PONV prophylaxis using the combination of haloperidol and dexamethasone compared to dexamethasone alone.[25]	Female patients between ages 20 – 65 years old with ASA classification I – II, non-smoking status, and use of IV PCA undergoing general anesthesia for gynecological laparoscopic surgery.[25] Sample size n = 150	Within 2 – 24 hours postoperatively, subjects in the haloperidol groups (1 mg and 2 mg) experienced less PONV, 22% and 20% respectively, in combination with dexamethasone, than the placebo group that scored a higher incidence of PONV at 42%.[25] Results after 24 hours demonstrated that there was a statistically significant difference at P = 0.003 in PONV incidence between haloperidol and dexamethasone combination treatment groups versus the control group, where 29%, 24%, and 54% of participants experienced PONV respectively.[25]	The 1 mg and 2 mg haloperidol doses were equally effective in preventing PONV when given in conjunction with dexamethasone and the combination of dexamethasone with haloperidol was more effective in PONV prevention than dexamethasone as a sole agent.[25]
Chaparro et al,[27] **(2010)**	To evaluate haloperidol's efficacy in PONV prophylaxis as an agent in combination therapy.[26]	Randomized double-blinded placebo-controlled trial. Quasi-experimental Level II	Randomized Double-blinded placebo-controlled trial evaluating PONV prophylaxis using combination of haloperidol and dexamethasone compared to dexamethasone as a sole agent.[26]	Non-smoking female patients between 18 – 50 years old with an ASA classification of I – II undergoing general anesthesia for an ambulatory plastic/ otorhinolaryngological procedure.[26]	There was no statistically significant protective effect for nausea prevention observed with the combination therapy at 6 and 24 hours, but the overall incidence of nausea was lower in the haloperidol with dexamethasone group at 22.5% and 41.5% respectively versus the dexamethasone group at	Participants who received dexamethasone without haloperidol experienced inferior PONV prophylaxis.[26]

				Sample size n = 166	27.5% and 52.5% respectively.[26] The incidence of vomiting was reduced at 6 hours and its decreased incidence became statistically significant at $P < 0.05$ at 24 hours with combination therapy.[26] At 6 hours, patients who received the combination therapy reported a lower incidence of vomiting at 15% versus dexamethasone alone at 26.25%.[26] At 24 hours, patients who received haloperidol and dexamethasone experienced a lower incidence of vomiting at 21.25% versus dexamethasone alone at 41.25%.[26]	
Chu et al,[28] (2008)	To investigate haloperidol's efficacy in PONV prophylaxis as an agent in combination therapy.[27]	Randomized, double-blinded, placebo, and positive-control study. Experimental study Level I	Randomized, double-blinded, placebo, and positive-control study evaluating PONV prophylaxis using combination of haloperidol and dexamethasone compared to dexamethasone, haloperidol,	Female patients with an ASA classification of I – II undergoing general anesthesia for laparoscopic-assisted vaginal hysterectomy.[27]	The statistically significant PONV incidences at $P < 0.05$ between 0 – 24 hours were the following in respective groups: 19% with haloperidol plus dexamethasone, 36% with droperidol, 37% with haloperidol, 38% with dexamethasone, and 65% with saline.[27]	Patients who received the combination of haloperidol and dexamethasone experienced superior PONV prophylaxis compared to other treatment groups.[27]

			droperidol, and saline as sole agents.[27]	Sample size n = 400		
Wang et al,[29] (2012)	To investigate dexamethasone's efficacy in PONV prophylaxis as an agent in combination therapy.[28]	Randomized clinical trial. Quasi-experimental study Level II	Randomized clinical trial comparing PONV prophylaxis of dexamethasone plus haloperidol with ondansetron plus dexamethasone.[28]	Female patients between 18 – 65 years old with an ASA classification of I – II undergoing general anesthesia for gynecologic, abdominal, and orthopedic surgeries expected to receive morphine PCA.[28] Sample size n = 135	The incidence of PONV among subjects that received dexamethasone plus ondansetron and dexamethasone plus haloperidol showed a significant difference at $P < 0.05$ when compared to those who only received dexamethasone.[28] Total PONV incidence after 24 hours in patients who only received dexamethasone was 25%, which was higher than in those who received dexamethasone plus haloperidol and dexamethasone plus ondansetron with an incidence of 15% and 13%, respectively.[28]	Both treatment groups that received haloperidol or ondansetron in combination with dexamethasone experienced diminished PONV incidence and there was less need for rescue anti-emetics over the course of 24 hours.[28] The sole treatment of PONV with dexamethasone was not as efficacious as combination therapy with haloperidol or ondansetron.[28]
Grecu et al,[30] (2008)	To investigate haloperidol's efficacy in PONV prophylaxis as an agent in	Randomized, double-blinded trial. Quasi-experimental study.	Randomized, double-blinded trial comparing the PONV efficacy of haloperidol in combination with ondansetron versus	Male and female patients with a high risk for PONV and at least 18 years old undergoing general anesthesia or combined general	Among patients who received haloperidol and ondansetron the following findings were significant: 90% with complete PONV response after 60 minutes, 76.2% complete PONV	Combination therapy with haloperidol and ondansetron provided a longer lasting and efficacious PONV prophylaxis versus ondansetron without

	combination therapy.[29]	Level II	ondansetron as a sole agent.[29]	anesthesia-epidural in a mixed surgical population.[29] Sample size n = 268	response after 480 minutes, 10% with nausea at 60 minutes or less, 23.9% with nausea at 480 minutes or less, 7.7% needing rescue at 180 minutes or less, and 20.8% needing rescue at 480 minutes or less.[29] In comparison, among patients who only received ondansetron, the following findings were significant: 66.2% with complete PONV response after 60 minutes, 59.2% with complete PONV response after 480 minutes, 33.8% with nausea at 60 minutes or less, 42.3% with nausea at 480 minutes or less, 24.1% needing rescue at 180 minutes or less, and 37.6% needing rescue at 480 minutes or less.[29] The time to rescue in those who received haloperidol plus ondansetron was 154.4 $\pm$ 133.8 minutes which was longer than ondansetron at 75.3 $\pm$ 82.8 minutes.[29]	haloperidol that was statistically significant with a *P* as low as < 0.001.[29]
Feng et al,[31] (2009)	To investigate haloperidol's efficacy in PONV	Randomized, double-blinded study.	Randomized, double-blinded study comparing the PONV efficacy	Male and female patients with an ASA classification of I – II undergoing	The total PONV incidence among patients who received haloperidol plus ondansetron was 21% at 0 – 24 hours;	The combination treatment of haloperidol and ondansetron yielded a

	prophylaxis as an agent in combination therapy.[30]	Quasi-experimental study. Level II	of haloperidol in combination with ondansetron compared to the sole use of each agent.[30]	general anesthesia for laparoscopic cholecystectomy.[30] Sample size n = 210	however, there was 39% at 0 – 24 hours for those who only received haloperidol and 38% at 0 – 24 hours for those who only received ondansetron.[30] The complete PONV response was 79% in the group that received haloperidol plus ondansetron; yet, 62% and 61% in subjects who received ondansetron and haloperidol respectively.[30]	greater PONV prevention response and an increase in patient satisfaction. Subjects who received both haloperidol and ondansetron suffered the lowest incidence of PONV and required less rescue analgesics or anti-emetics.[30]
Dağ et al,[32] (2019)	To evaluate the most efficacious dose of haloperidol for PONV prophylaxis with the least amount of side effects.[31]	Randomized controlled trial. Experimental study Level I	Randomized controlled trial comparing PONV efficacy of haloperidol doses of 0.25 mg, 0.5 mg, 1 mg, and 2 mg to a saline placebo.[31]	Female patients between the ages of 19 and 70 years with an ASA classification of I – II undergoing general anesthesia for laparoscopic abdominal hysterectomy.[31] Sample size n = 250	The incidence of nausea differed 2 hours postoperatively and was recorded as statistically significant at $P > 0.008$; 28% of patients in group V given 0.25 mg of haloperidol, 14% of patients in group IV given 0.5 mg of haloperidol, 14% in group III given 1 mg of haloperidol, 4% of patients in group II given 2 mg of haloperidol, and 26% of patients in group I given the placebo had nausea.[31] There was also a statistically significant difference at $P = 0.000$ of nausea incidence between 2 and 24 hours after	There was a statistically significant difference among treatment groups; the placebo group experienced the highest anti-emetic need at 40% while the subjects treated with haloperidol required fewer rescue anti-emetics.[31] The optimal and efficacious dosages of parenteral haloperidol for PONV range from 0.5 mg to 2 mg.[31] Participants in group II who received the

					surgery; 28% of patients in group V given 0.25 mg of haloperidol, 6% of patients in group IV given 0.5 mg of haloperidol, 2% in group III given 1 mg of haloperidol, 4% of patients in group II given 2 mg of haloperidol, and 18% of patients in group I given the placebo had nausea.[31] Two hours postoperatively, researchers observed a statistically significant difference at $P = 0.009$ among groups regarding the incidence of vomiting; 16% of patients in group V given 0.25 mg of haloperidol, 10% of patients in group IV given 0.5 mg of haloperidol, 6% in group III given 1 mg of haloperidol, 0% of patients in group II given 2 mg of haloperidol, and 20% of patients in group I given the placebo experienced vomiting.[31] Between 2 and 24 hours after surgery, groups did not show a statistically significant difference at $P = 0.218$ in regards to the incidence of vomiting. It was reported	highest dose of haloperidol of 2 mg experienced the highest level of patient satisfaction that was also statistically significant at $P < 0.05$.[31]

					that 6% of participants who received 2 mg of haloperidol in group II, 8% of participants who received 1 mg of haloperidol in group III, 14% of participants who received 0.5 mg of haloperidol in group IV, and 28% of participants who received 0.25 mg of haloperidol in group V needed an additional anti-emetic, which was statistically significant at $P < 0.05$.[31]	

Appendix B: QI Project IRB Exemption

FIU | FLORIDA INTERNATIONAL UNIVERSITY

Office of Research Integrity
Research Compliance, MARC 414

Xenia Del Pozo

EJ

April 6, 2022

"An Educational Module on the Utilization of Haloperidol as a Pharmacological Compliment for Postoperative Nausea and Vomiting Prophylaxis in Adult Surgical Patients"

IRB-22-0133 04/06/22
111521

As a requirement of IRB Exemption you are required to:

1) Submit an IRB Exempt Amendment Form for all proposed additions or changes in the procedures involving human subjects. All additions and changes must be reviewed and approved prior to implementation.
2) Promptly submit an IRB Exempt Event Report Form for every serious or unusual or unanticipated adverse event, problems with the rights or welfare of the human subjects, and/or deviations from the approved protocol.

or

discontinued.

Special Conditions: N/A

For further information, you may visit the IRB website at http://research.fiu.edu/irb.

EJ

Appendix C: QI Project Consent

Nicole Wertheim College of Nursing & Health Sciences

CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT

"An Educational Module on the Utilization of Haloperidol as a Pharmacological Complement for Postoperative Nausea and Vomiting Prophylaxis in Adult Surgical Patients"

SUMMARY INFORMATION

Things you should know about this quality improvement project:

- **Purpose:** Educational module to increase anesthesia provider knowledge and attitude on the utilization of haloperidol as a pharmacological complement for postoperative nausea and vomiting prophylaxis in adult general anesthesia patients.
- **Procedures**: If you choose to participate, you will be asked to complete a pre-test, watch a voice over PowerPoint, and then a post-test.
- **Duration:** This will take about a total of 25 minutes.
- **Risks**: The main risks for this quality improvement project are minimal. As with any educational module, potential minimal risks are mild emotional stress or physical discomfort from sitting on a chair for an extended period of time.
- **Benefits:** The main benefit to you from this educational module is an increase in participant knowledge and attitude in utilizing haloperidol as a pharmacological complement for postoperative nausea and vomiting prophylaxis in adult surgical patients.
- **Alternatives:** There are no known alternatives available to you other than not taking part in this study.
- **Participation:** Taking part in this quality improvement project is voluntary. If you decide to participate you will be 1 of 10 participants.

Please carefully read the entire document before agreeing to participate.

PURPOSE OF THE PROJECT

You are being asked to be in a quality improvement project. The goal of this project is to increase anesthesia provider knowledge and attitude on the utilization of haloperidol as a pharmacological complement for postoperative nausea and vomiting prophylaxis in adult surgical patients.

DURATION OF THE PROJECT

Your participation will require about 25 minutes of your time. If you decide to participate you will be 1 of 10 participants.

PROCEDURES

If you agree to be in the project, we will ask you to do the following things:

1. Complete an online 16 question pre-test survey via Qualtrics, an Online survey product for which the URL link is provided.
2. Review the educational PowerPoint Module lasting 22 minutes.
3. Complete the online 16 question post-test survey via Qualtrics, an Online survey product for which the URL link is provided.

RISKS AND/OR DISCOMFORTS

The main risks for this quality improvement project are minimal. As with any educational module, potential minimal risks are mild emotional stress or physical discomfort from sitting on a chair for an extended period of time.

BENEFITS

The following benefits may be associated with your participation in this project: An increased understanding of the role of haloperidol as a pharmacologic complement for postoperative nausea and vomiting (PONV) prophylaxis in adult surgical patients. The overall objective of the program is to improve the perioperative patient experience by diminishing the incidence of PONV.

ALTERNATIVES

There are no known alternatives available to you other than not taking part in this project. However, if you would like to receive the educational material given to the participants in this project, it will be provided to you at no cost.

CONFIDENTIALITY

The records of this project will be kept private and will be protected to the fullest extent provided by law. If, in any sort of report, we might publish, we will not include any information that will make it possible to identify you as a participant. Records will be stored securely, and only the project team will have access to the records.

PARTICIPATION: Taking part in this research project is voluntary.

COMPENSATION & COSTS

here is no cost or payment to you for receiving the health education and/or for participating in this project.

RIGHT TO DECLINE OR WITHDRAW

Your participation in this project is voluntary. You are free to participate in the project or withdraw your consent at any time during the project. Your withdrawal or lack of participation will not affect any benefits to which you are otherwise entitled. The investigator reserves the right to remove you without your consent at such time that they feel it is in the best interest.

RESEARCHER CONTACT INFORMATION

If you have any questions about the purpose, procedures, or any other issues relating to this research project, you may contact Xenia Del Pozo at 305-439-8058 at xdelp002@fiu.edu and Dr. Ann Miller at 305-348-4871 anmille@fiu.edu.

IRB CONTACT INFORMATION

If you would like to talk with someone about your rights pertaining to being a subject in this project or about ethical issues with this project, you may contact the FIU Office of Research Integrity by phone

at 305-348-2494 or by email at ori@fiu.edu.

PARTICIPANT AGREEMENT

I have read the information in this consent form and agree to participate in this study. I have had a chance to ask any questions I have about this study, and they have been answered for me. By clicking on the "consent to participate" button below I am providing my informed consent.

Appendix D: QI Project Letter of Support

Envision
PHYSICIAN SERVICES

February 2nd, 2022

Ann B. Miller, DNP, CRNA, APRN
Clinical Associate Professor
Department of Nurse Anesthesiology
Florida International University

Dr. Miller,

Thank you for inviting Memorial Regional to participate in Doctor of Nursing Practice (DNP) project conducted by Xenia Del Pozo entitled "An Educational Module on the Utilization of Haloperidol as a pharmacological Compliment for Postoperative Nausea and Vomiting Prophylaxis in Adult Surgical Paitents" in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthetist Practice at Florida International University. I have warranted Ms. Del Pozo permission to conduct the project using our providers.

Evidence-based practice's primary aim is to yield the best outcomes for patients by selecting interventions supported by the evidence. This project intends to evaluate if the utilization of preoperative airway ultrasonography increases providers knowledge to predict difficult intubations.

We understand that participation in the study is voluntary and carries no overt risk. All Anesthesiology providers are free to participate or withdraw from the study at any time. The educational intervention will be conveyed by a 15-minute virtual PowerPoint presentation, with a pretest and posttest questionnaire delivered by a URL link electronically via Qualtrics, an online survey product. Responses to pretest and posttest surveys are not linked to any participant. The collected information is reported as an aggregate, and there is no monetary compensation for participation. All collected material will be kept confidential, stored in a password encrypted digital cloud, and only be accessible to the investigators of this study: Xenia Del Pozo and Ann B. Miller. We expect that Xenia Del Pozo will not interfere with normal hospital performance, behaving in a professional manner and following standards of care.

Prior to the implementation of this educational project the Florida International University Institutional Review Board will evaluate and approve the procedures to conduct this project. Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. We support the participation of our Anesthesiology providers in this project and look forward to working with you.

Suzanne Hale

Suzanne Hale, MSN, CRNA, ARNP
Advanced Practice Provider Director, Broward and Dade
Chief, Memorial Regional Hospital
Envision Physician Services
954-265-2044

3501 Johnson Street | Hollywood, FL 33021

Appendix E: QI Project Pre-test and Post-test Survey

Nicole Wertheim College of Nursing & Health Sciences

Pre-test and Post-test Questionnaire:

An Educational Module on the Utilization of Haloperidol as a Pharmacological Complement for Postoperative Nausea and Vomiting Prophylaxis in Adult Surgical Patients

INTRODUCTION

The primary aim of this QI project is to improve the knowledge and attitudes of anesthesia providers pertaining to the utilization of haloperidol in combination pharmacologic therapy during the perioperative period to decrease the incidence of PONV.

Please answer the questions below to the best of your ability. The questions include demographic information and knowledge of haloperidol utilization in adult surgical patients. Questions are either in multiple choice or likert style format and are meant to measure anesthesia provider knowledge of the efficacy of haloperidol for PONV prophylaxis and the respective attitude of its application in practice.

PERSONAL INFORMATION

1. **Gender:** Male Female Other _____
2. **Age:** _____
3. **Ethnicity:**

   Hispanic Caucasian African American Other _____
4. **Position/Title**: _____

5. **Level of education:** Associates Bachelors Masters Doctoral (DNP, DNAP, MD, EdD)
6. **Years of experience:** Less than 1 year 1 to 5 6 to 10 more than 10 years

QUESTIONNAIRE

1. **The incidence of postoperative nausea and vomiting can be as high as:**
    a. 80%
    b. 60%
    c. 40%
    d. 20%

    CORRECT ANSWER: a.
2. **What is the most efficacious parenteral dose range of haloperidol for PONV prophylaxis according to most recent literature?**
    a. 2 – 4 mg
    b. 0.5 – 2 mg
    c. 0.2 – 0.5 mg
    d. 0.2 – 0.7 mg

    CORRECT ANSWER: b.
3. **What classification of anti-emetic is haloperidol considered?**
    a. NK-1 receptor antagonist
    b. Antihistamine
    c. Dopamine D2 receptor antagonist
    d. Serotonin 5-HT3 receptor antagonist

    CORRECT ANSWER: c.

4. **Haloperidol's clinical effects can be attributed to what mechanism(s) of action? (Select all that apply)**

    a. Works at the area postrema and chemoreceptor trigger zone (CTZ) as D2 receptor antagonist

    b. Sedative properties

    c. Blocks dopamine receptors via inhibition of dopamine production on cyclic adenosine monophosphate (cAMP)

    d. Alpha-adrenergic inhibiting properties

    e. All of the above

    CORRECT ANSWER: e.

5. **What population of surgical patients can benefit from PONV prophylaxis with haloperidol? (Select all that apply)**

    a. Patients undergoing otorhinolaryngological procedures

    b. Patients undergoing ophthalmic procedures

    c. Patients undergoing laparoscopic procedures

    d. Patients undergoing gynecological procedures

    e. All of the above

    CORRECT ANSWER: e.

6. **What are unpleasant symptoms associated with PONV contributing to considerable patient morbidity and distress? (Select all that apply)**

    a. Esophageal rupture

    b. Wound dehiscence

    c. Aspiration

d. Dehydration

e. All of the above

CORRECT ANSWER: e.

7. **Haloperidol should be excluded from patients presenting with which disease process(es) or condition(s)? (Select all that apply)**

    a. Parkinson's disease

    b. Neuroleptic malignant syndrome (NMS)

    c. Acute/chronic dysrhythmias

    d. QT prolongation

    e. All of the above

    CORRECT ANSWER: e.

8. **Potential side effects of haloperidol at high dosages, such as 35 mg or more, include (Select 2).**

    a. QT prolongation

    b. Hypertension

    c. Torsades de pointes

    d. Photophobia

    CORRECT ANSWERS: a. & c.

9. **Utilization of haloperidol in combination with what other medications have shown superior PONV prophylaxis? (Select 2)**

    a. Dexamethasone

    b. Promethazine

    c. Ondansetron

d. Droperidol

CORRECT ANSWERS: a. & c.

10. **PONV prophylaxis is most efficacious when haloperidol is administered when intraoperatively?**

    a. At induction

    b. At incision

    c. At the termination of surgery

    d. At any time

    CORRECT ANSWER: d.

11. **What is haloperidol's onset of action for PONV prophylaxis?**

    a. 15 minutes

    b. 30 minutes

    c. 45 minutes

    d. 60 minutes

    CORRECT ANSWER: b.

12. **What is haloperidol's duration of action for PONV prophylaxis?**

    a. 4 hours

    b. 3 hours

    c. 2 hours

    d. 1 hour

    CORRECT ANSWER: a.

13. **What is haloperidol's elimination half-life?**

    a. 2 – 4 hours

b. 4 – 6 hours

c. 6 – 12 hours

d. 12 – 35 hours

CORRECT ANSWER: d.

14. **How likely are you to administer haloperidol in combination therapy for PONV prophylaxis?**

    a. Most likely

    b. Somewhat likely

    c. Somewhat unlikely

    d. Most unlikely

15. **What is your attitude toward the administration of haloperidol as a complementary drug to decrease PONV?**

    a. Very positive

    b. Positive

    c. Neutral

    d. Negative

    e. Very negative

16. **How likely are you to implement haloperidol into your anesthesia practice?**

    a. Very likely

    b. Likely

    c. Unsure

    d. Unlikely

    e. Very unlikely

Appendix F: QI Project Educational Module

An Educational Module on the Utilization of Haloperidol as a Pharmacological Complement for Postoperative Nausea and Vomiting Prophylaxis in Adult Surgical Patients

XENIA DEL POZO, BSN, RN, SRNA
ANN B. MILLER, DNP, CRNA, APRN

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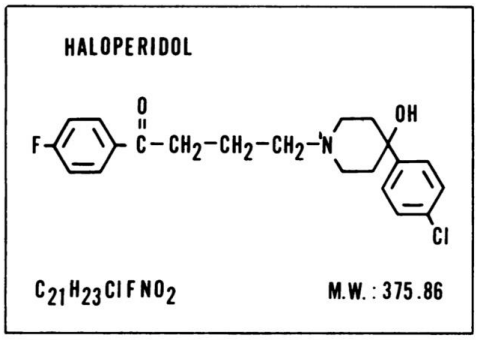
Learning Objectives

- *From this quality improvement project, the student will:*
  - Describe postoperative nausea and vomiting (PONV) risk factors
  - Discuss mechanism of action of Haloperidol
  - Understand recently studied anti-emetics available for PONV prophylaxis
  - Formulate the most efficacious pharmacologic combinations of anti-emetics used for PONV prophylaxis
  - Formulate PONV prophylaxis algorithms and guidelines for adult surgical patients



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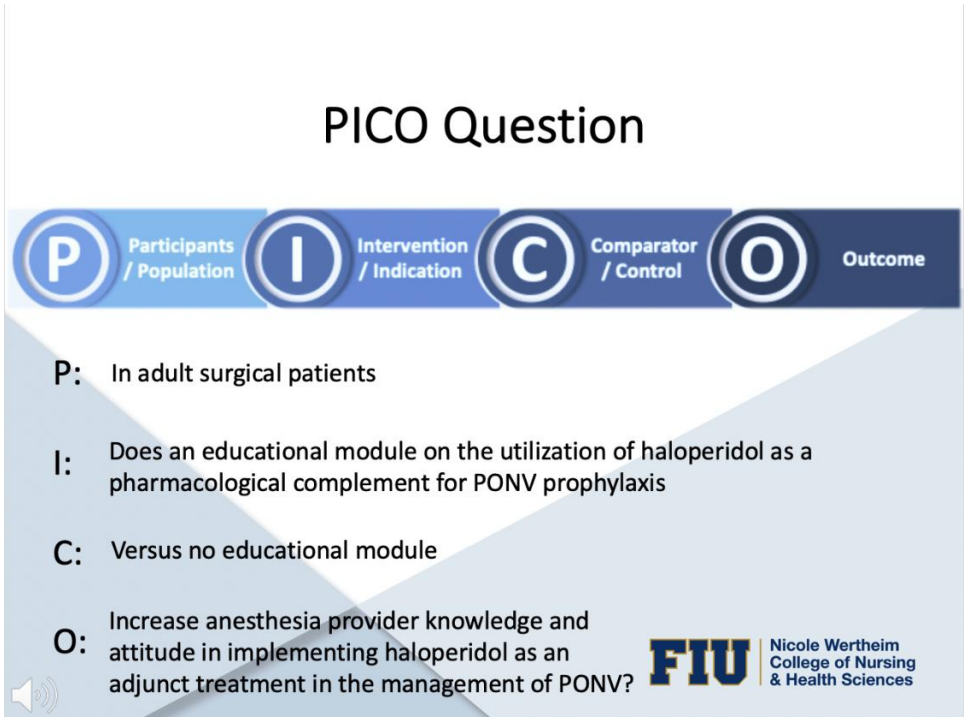
PICO Question
P Participants / Population
I Intervention / Indication
C Comparator / Control
O Outcome
P: In adult surgical patients
I: Does an educational module on the utilization of haloperidol as a pharmacological complement for PONV prophylaxis
C: Versus no educational module
O: Increase anesthesia provider knowledge and attitude in implementing haloperidol as an adjunct treatment in the management of PONV?
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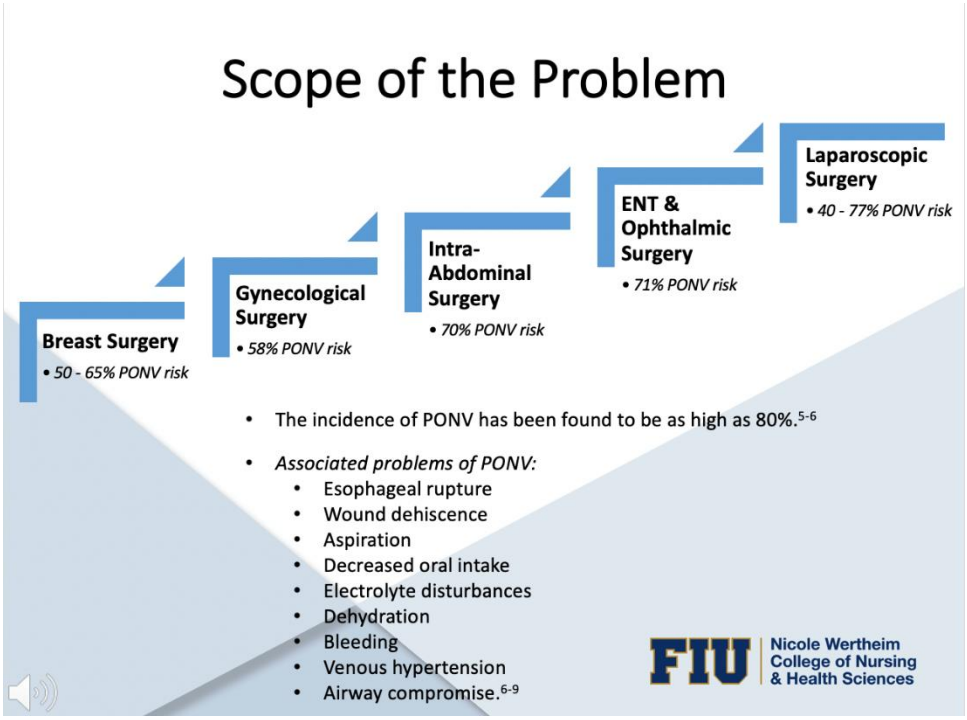
Scope of the Problem
Breast Surgery
• 50 - 65% PONV risk
Gynecological Surgery
• 58% PONV risk
Intra-Abdominal Surgery
• 70% PONV risk
ENT & Ophthalmic Surgery
• 71% PONV risk
Laparoscopic Surgery
• 40 - 77% PONV risk
• The incidence of PONV has been found to be as high as 80%.[5-6]
• Associated problems of PONV:
• Esophageal rupture
• Wound dehiscence
• Aspiration
• Decreased oral intake
• Electrolyte disturbances
• Dehydration
• Bleeding
• Venous hypertension
• Airway compromise.[6-9]
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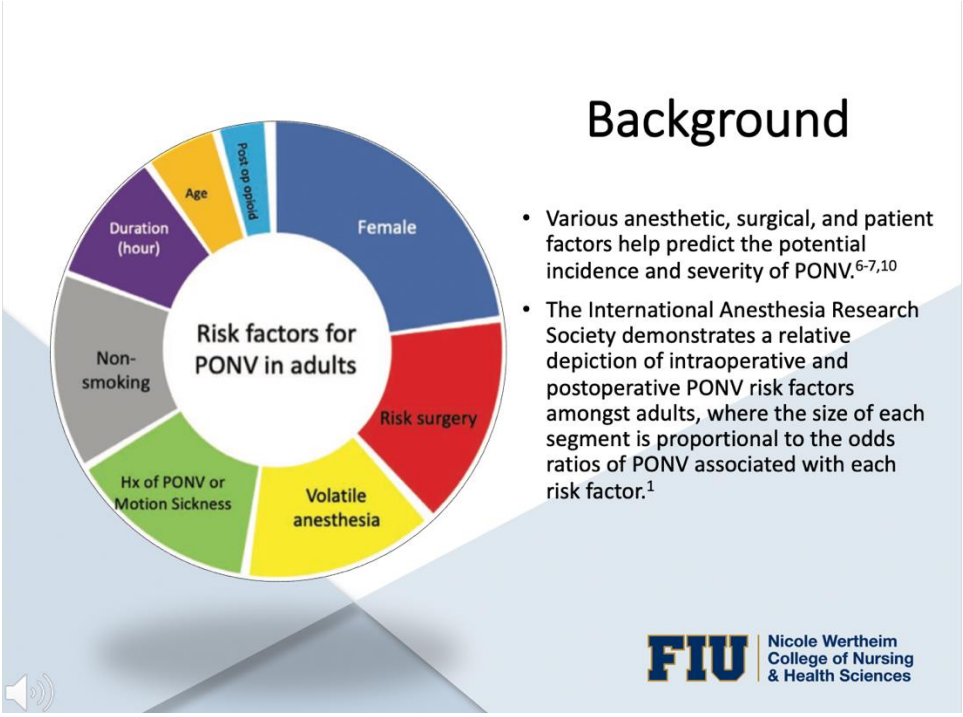
Background
Risk factors for PONV in adults
Female
Risk surgery
Volatile anesthesia
Hx of PONV or Motion Sickness
Non-smoking
Duration (hour)
Age
Post op opioid
• Various anesthetic, surgical, and patient factors help predict the potential incidence and severity of PONV.[6-7,10]
• The International Anesthesia Research Society demonstrates a relative depiction of intraoperative and postoperative PONV risk factors amongst adults, where the size of each segment is proportional to the odds ratios of PONV associated with each risk factor.[1]
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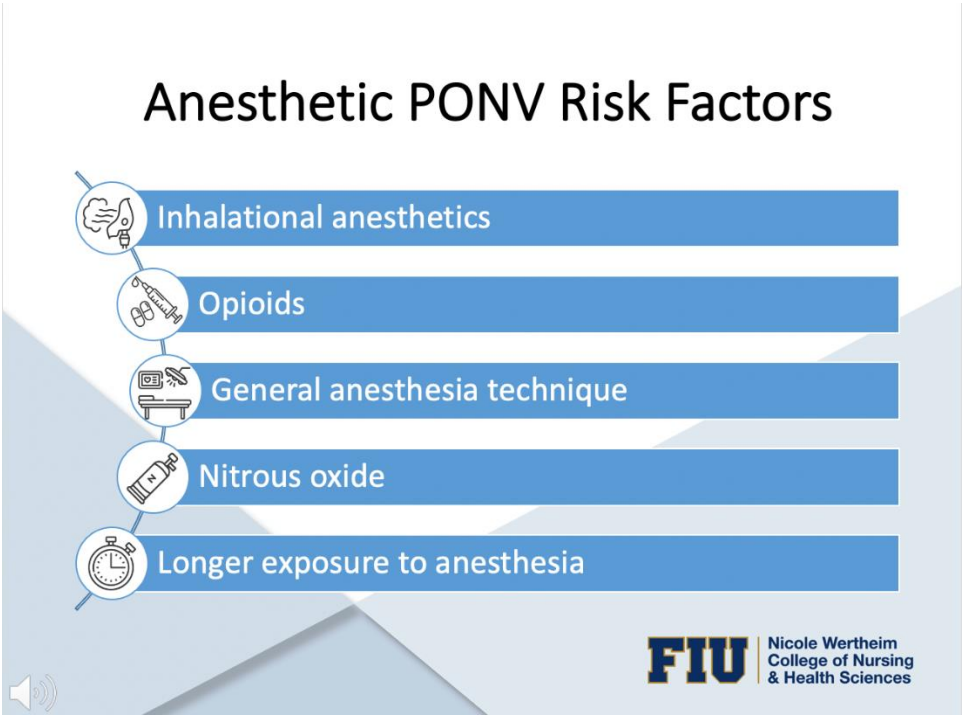
Anesthetic PONV Risk Factors
Inhalational anesthetics
Opioids
General anesthesia technique
Nitrous oxide
Longer exposure to anesthesia
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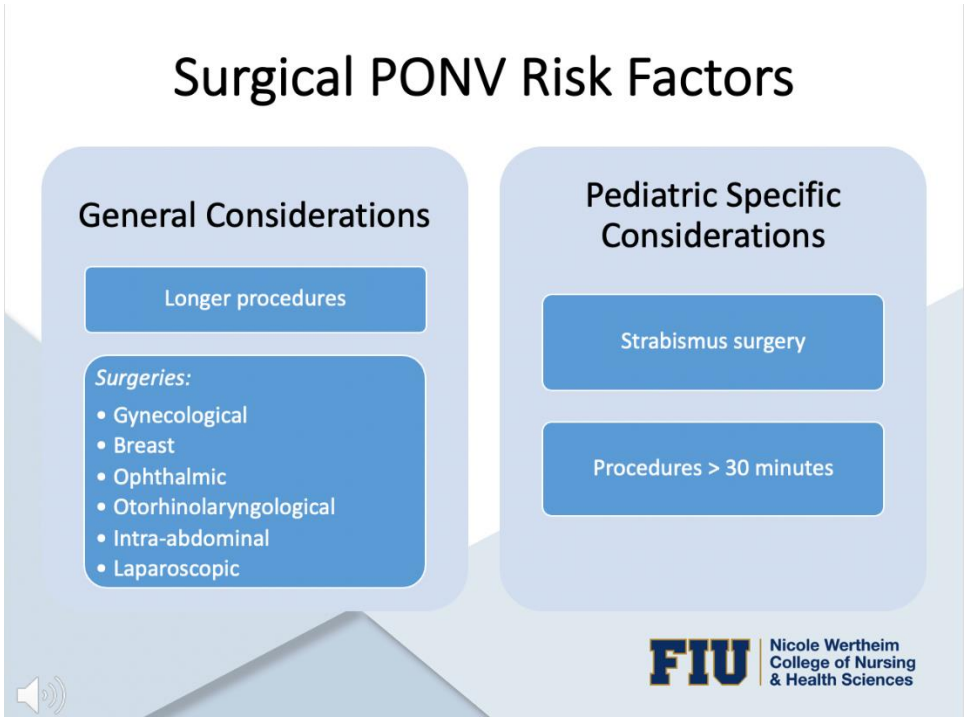
Surgical PONV Risk Factors
General Considerations
Longer procedures
Surgeries:
• Gynecological
• Breast
• Ophthalmic
• Otorhinolaryngological
• Intra-abdominal
• Laparoscopic
Pediatric Specific Considerations
Strabismus surgery
Procedures > 30 minutes
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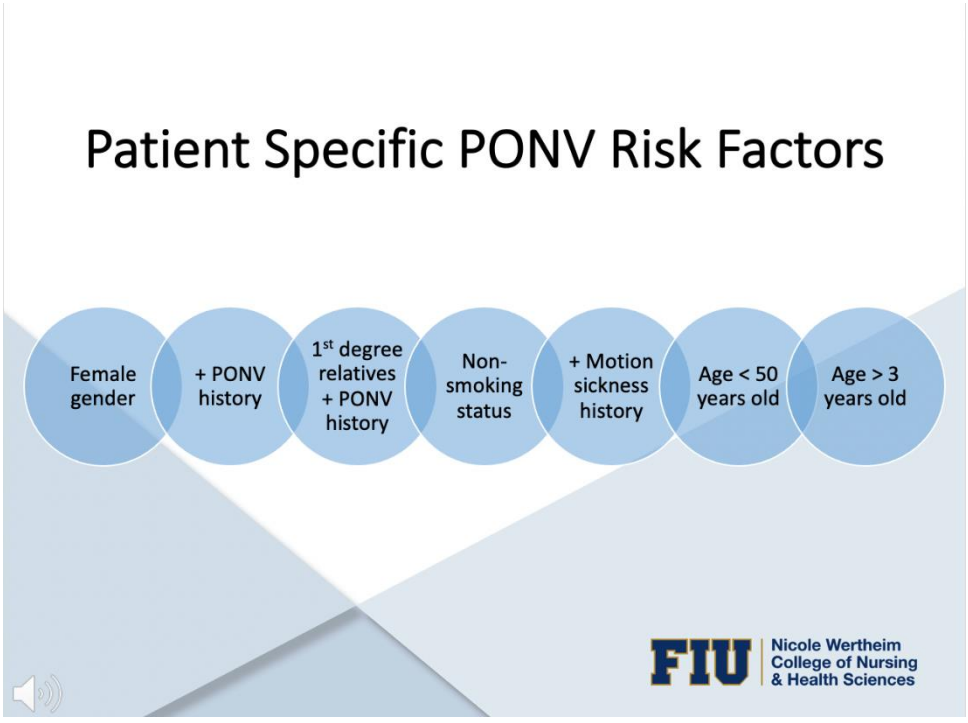
Patient Specific PONV Risk Factors
Female gender
+ PONV history
1st degree relatives + PONV history
Non-smoking status
+ Motion sickness history
Age < 50 years old
Age > 3 years old
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PONV Medication Classifications

Newer Generation

- Serotonin receptor antagonists
- NK-1 receptor antagonists

Non-traditional

- Corticosteroids

Older Generation

- Phenothiazines
- Antihistamines
- Anticholinergics
- Benzamides
- Butyrophenones

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Adults
- 5-HT_3 receptor antagonists + dexamethasone
  - Ondansetron: (A1)[158,159]
  - Palonosetron: (A2)[160–164]
  - Ramosetron: (A2)[165,166]
  - Granisetron: (A3)[167]
  - Tropisetron: (A3)[168]; with methylprednisolone (A3)[169]
- 5-HT_3 receptor antagonists + aprepitant
  - Ondansetron: (A2)[170,171]
  - Ramosetron: (A3)[172]
  - Palonosetron: (A3)[173]

Aprepitant + dexamethasone: (A2)[174,175]
- 5-HT_3 + droperidol
  - Ondansetron + droperidol: (A3)[176]
  - Granisetron + droperidol: (A3)[177]
  - Palonosetron + droperidol: (A3)[178]
- Other 5-HT_3 combination therapies:
  - Ondansetron + haloperidol: (A3)[179]
  - Haloperidol + dexamethasone + ondansetron: (A3)[180]
  - Ondansetron + betahistine: (A2)[181,182]
  - Ramosetron + gabapentin: (A3)[183]
  - Midazolam + ramosetron: (A3)[184]
- Other antidopaminergic combination therapies
  - Dexamethasone + haloperidol: (A2)[185,186]
  - Metoclopramide + dimenhydrinate: (A3)[187]
  - Amisulpride +1 nondopaminergic antiemetic: (A3)[188]
  - Haloperidol + midazolam: (A2)[189,190]

Acupoint stimulation + pharmacoprophylaxis: (A2)[191,192]
- Others
  - Propofol + dexamethasone: (A3)[193]
  - Dexamethasone + dimenhydrinate:[194] (A3)
  - Gabapentin + dexamethasone: (A3)[195]

Children
- Ondansetron + dexamethasone: (A1)[196]
- Ondansetron + droperidol (A3)[197]
- Tropisetron + dexamethasone (A3)[198]

Abbreviation: 5-HT_3, 5-hydroxytryptamine 3.

Combination Drug Therapy

- Research advocates for the utilization of combination therapy for PONV prophylaxis with the understanding that antagonizing multiple receptors associated with PONV can provide superior PONV prevention in surgical patients.[1,3-4,11]
- The International Anesthesia Research Society summarizes common combinations of anti-emetics recommended for PONV pharmacologic combination therapy for adults and children.[1]

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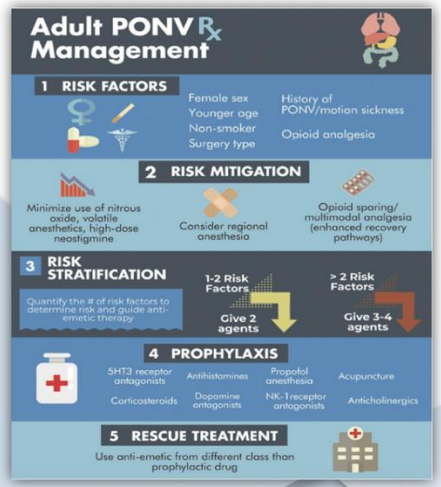
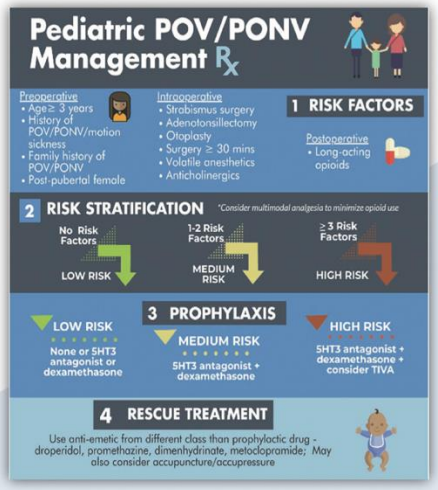
International Anesthesia Research Society 2020 PONV Guidelines





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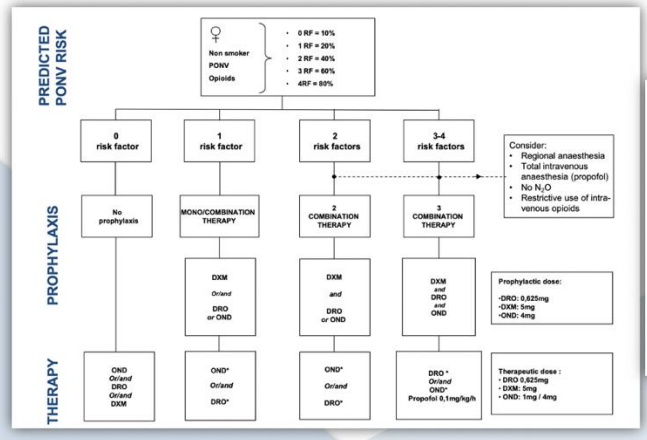
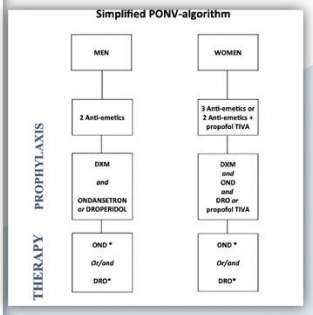
British Journal of Anesthesia 2018 PONV Algorithms





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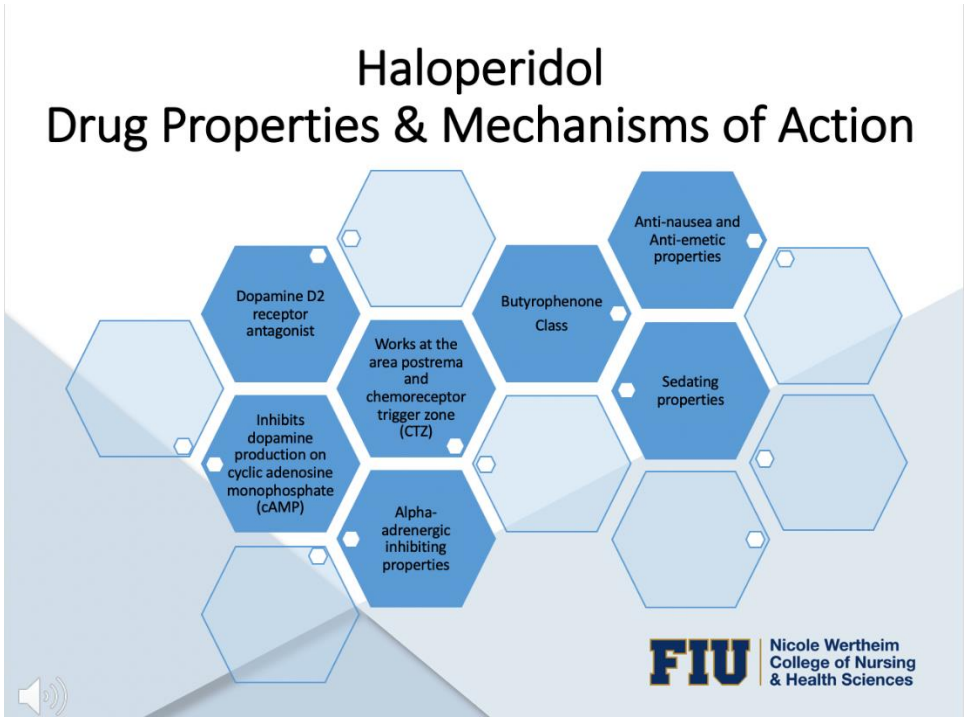
Haloperidol
Drug Properties & Mechanisms of Action
Dopamine D2 receptor antagonist
Works at the area postrema and chemoreceptor trigger zone (CTZ)
Butyrophenone Class
Anti-nausea and Anti-emetic properties
Sedating properties
Inhibits dopamine production on cyclic adenosine monophosphate (cAMP)
Alpha-adrenergic inhibiting properties
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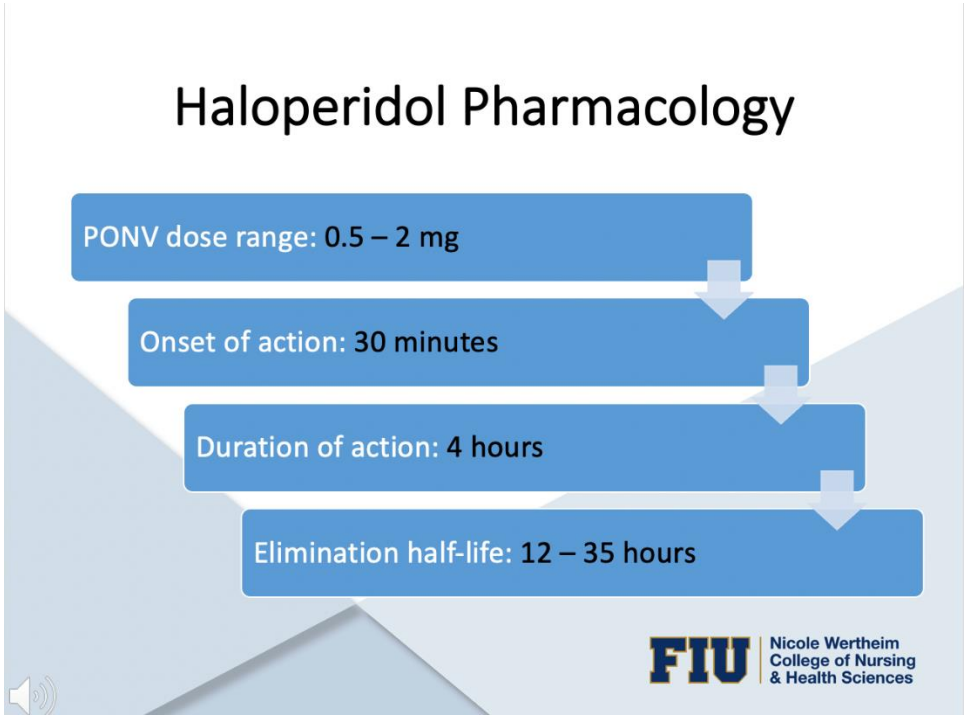
Haloperidol Pharmacology
PONV dose range: 0.5 – 2 mg
Onset of action: 30 minutes
Duration of action: 4 hours
Elimination half-life: 12 – 35 hours
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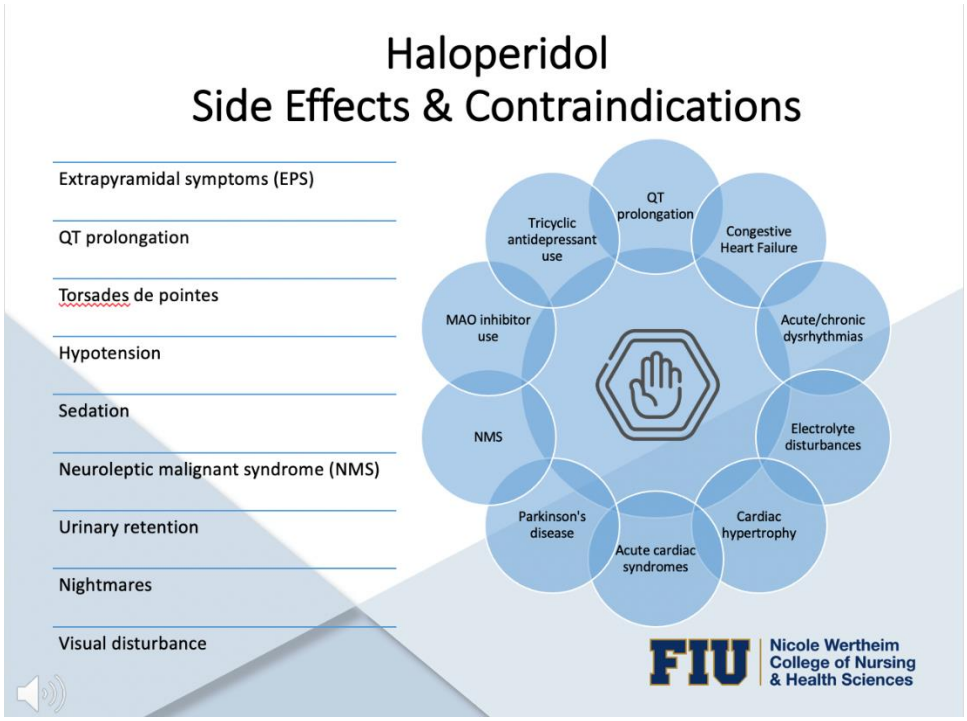
Haloperidol
Side Effects & Contraindications
Extrapyramidal symptoms (EPS)
QT prolongation
Torsades de pointes
Hypotension
Sedation
Neuroleptic malignant syndrome (NMS)
Urinary retention
Nightmares
Visual disturbance
QT prolongation
Congestive Heart Failure
Acute/chronic dysrhythmias
Electrolyte disturbances
Cardiac hypertrophy
Acute cardiac syndromes
Parkinson's disease
NMS
MAO inhibitor use
Tricyclic antidepressant use
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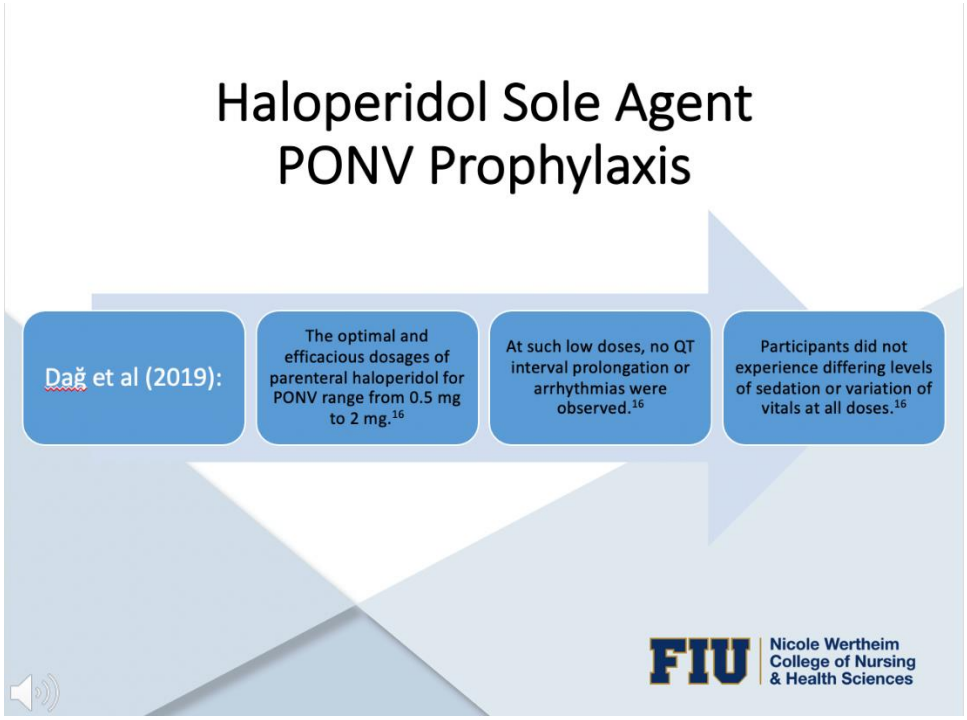
Haloperidol Sole Agent
PONV Prophylaxis
Dağ et al (2019):
The optimal and efficacious dosages of parenteral haloperidol for PONV range from 0.5 mg to 2 mg.[16]
At such low doses, no QT interval prolongation or arrhythmias were observed.[16]
Participants did not experience differing levels of sedation or variation of vitals at all doses.[16]
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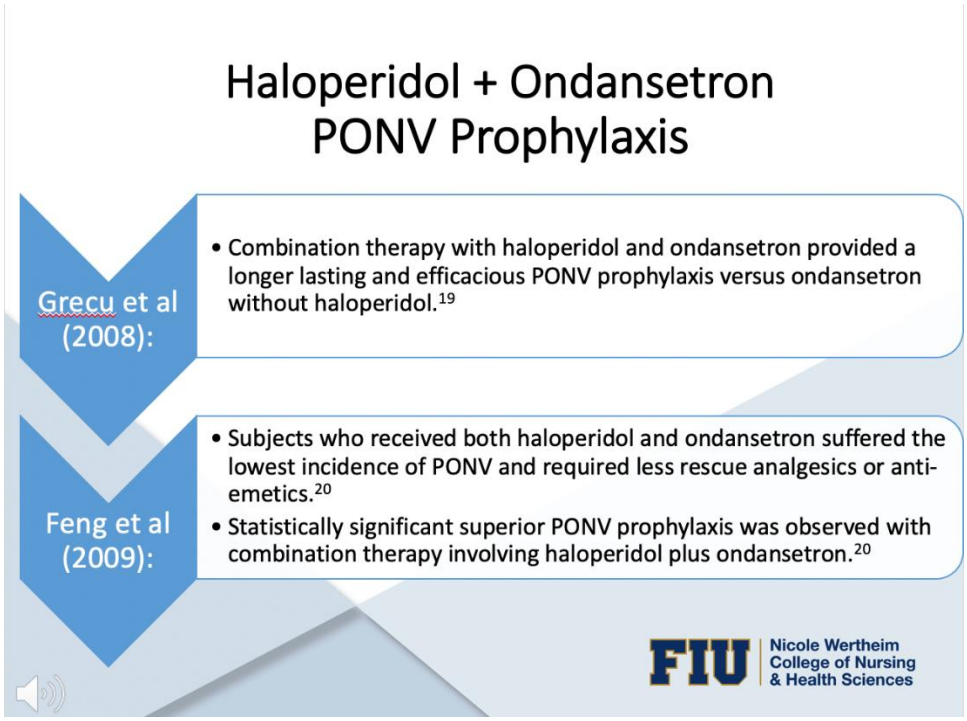
Haloperidol + Ondansetron
PONV Prophylaxis
Grecu et al (2008):
• Combination therapy with haloperidol and ondansetron provided a longer lasting and efficacious PONV prophylaxis versus ondansetron without haloperidol.[19]
Feng et al (2009):
• Subjects who received both haloperidol and ondansetron suffered the lowest incidence of PONV and required less rescue analgesics or anti-emetics.[20]
• Statistically significant superior PONV prophylaxis was observed with combination therapy involving haloperidol plus ondansetron.[20]
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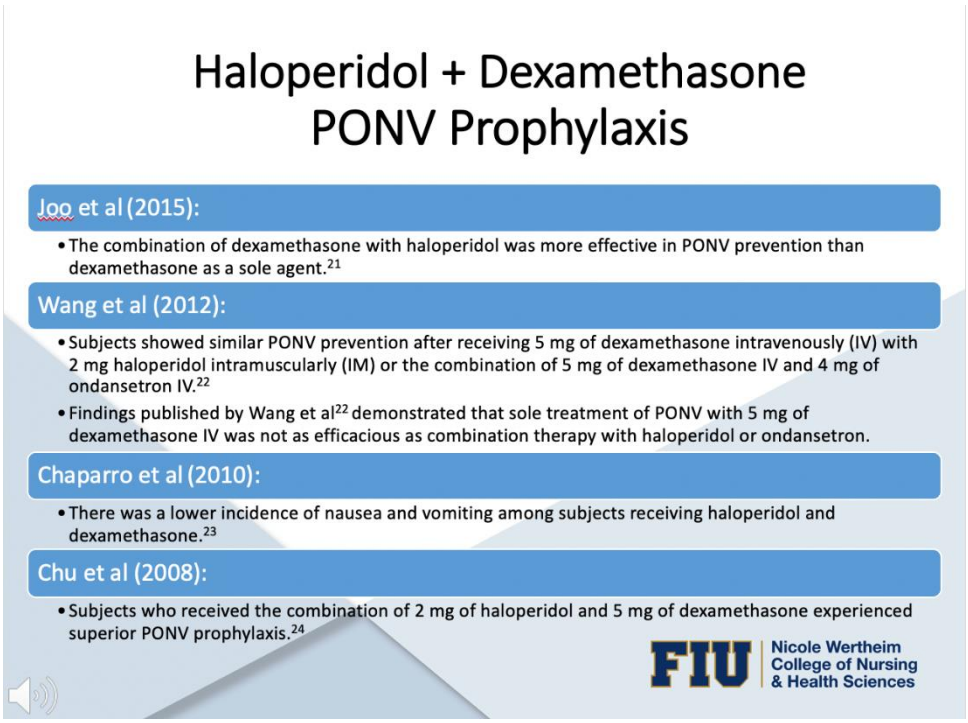
Haloperidol + Dexamethasone
PONV Prophylaxis
Joo et al (2015):
• The combination of dexamethasone with haloperidol was more effective in PONV prevention than dexamethasone as a sole agent.[21]
Wang et al (2012):
• Subjects showed similar PONV prevention after receiving 5 mg of dexamethasone intravenously (IV) with 2 mg haloperidol intramuscularly (IM) or the combination of 5 mg of dexamethasone IV and 4 mg of ondansetron IV.[22]
• Findings published by Wang et al[22] demonstrated that sole treatment of PONV with 5 mg of dexamethasone IV was not as efficacious as combination therapy with haloperidol or ondansetron.
Chaparro et al (2010):
• There was a lower incidence of nausea and vomiting among subjects receiving haloperidol and dexamethasone.[23]
Chu et al (2008):
• Subjects who received the combination of 2 mg of haloperidol and 5 mg of dexamethasone experienced superior PONV prophylaxis.[24]
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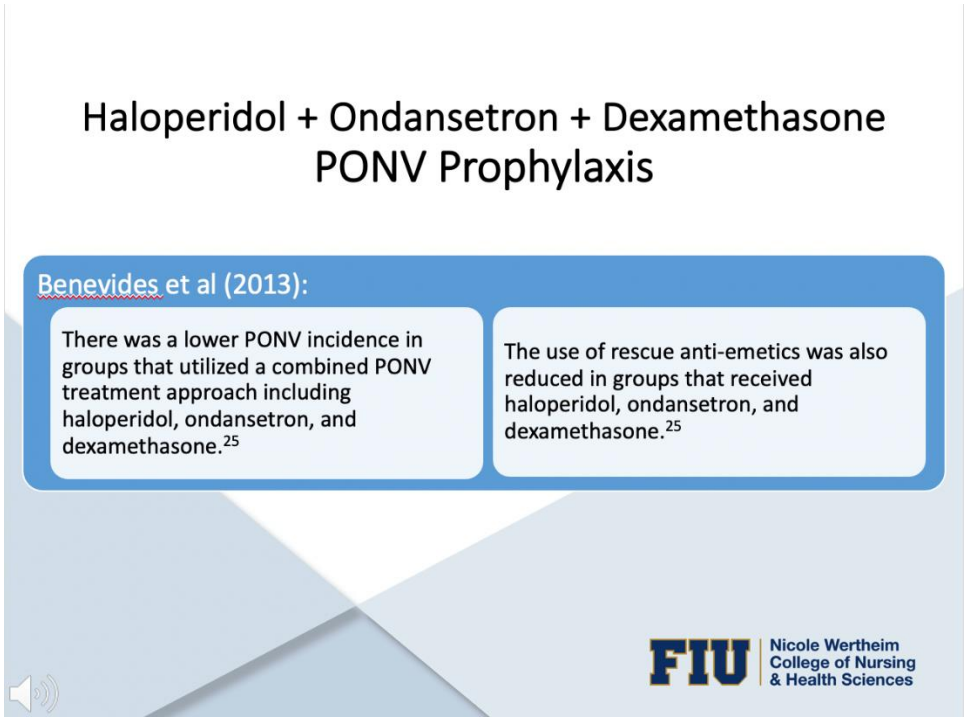
Haloperidol + Ondansetron + Dexamethasone
PONV Prophylaxis
Benevides et al (2013):
There was a lower PONV incidence in groups that utilized a combined PONV treatment approach including haloperidol, ondansetron, and dexamethasone.25
The use of rescue anti-emetics was also reduced in groups that received haloperidol, ondansetron, and dexamethasone.25
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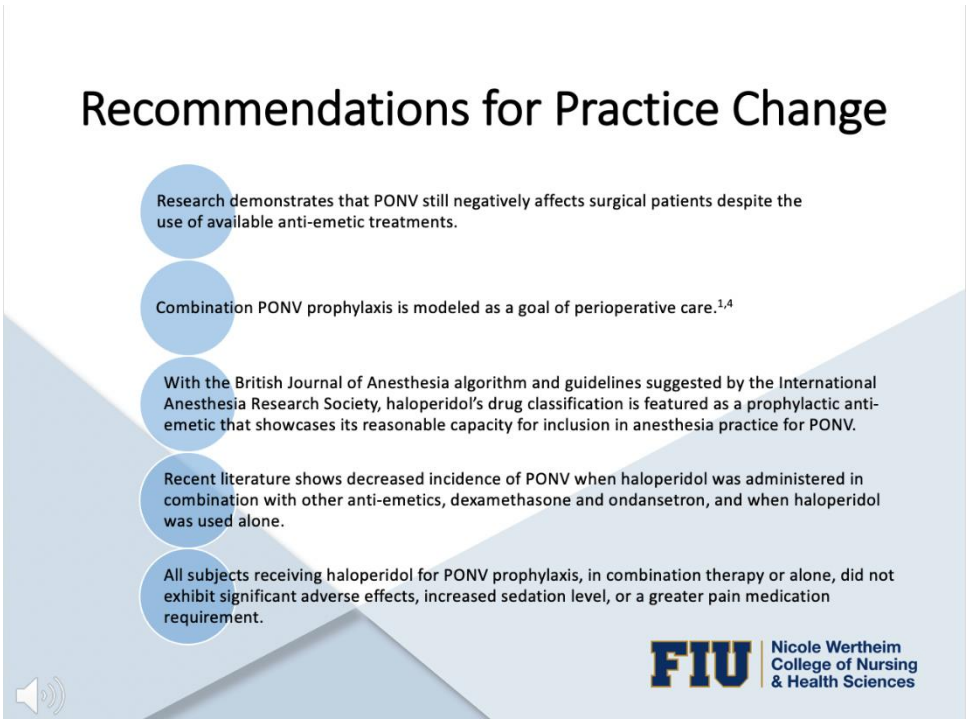
Recommendations for Practice Change
Research demonstrates that PONV still negatively affects surgical patients despite the use of available anti-emetic treatments.
Combination PONV prophylaxis is modeled as a goal of perioperative care.1,4
With the British Journal of Anesthesia algorithm and guidelines suggested by the International Anesthesia Research Society, haloperidol's drug classification is featured as a prophylactic anti-emetic that showcases its reasonable capacity for inclusion in anesthesia practice for PONV.
Recent literature shows decreased incidence of PONV when haloperidol was administered in combination with other anti-emetics, dexamethasone and ondansetron, and when haloperidol was used alone.
All subjects receiving haloperidol for PONV prophylaxis, in combination therapy or alone, did not exhibit significant adverse effects, increased sedation level, or a greater pain medication requirement.
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