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The Use of Aprepitant versus Ondansetron in the Prevention of Postoperative Nausea and Vomiting (PONV) in Adult Patients Undergoing General Anesthesia

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The Use of Aprepitant versus Ondansetron in the Prevention of Postoperative Nausea and Vomiting (PONV) in Adult Patients Undergoing General Anesthesia

A DNP Project Presented to the Faculty of the
Nicole Wertheim College of Nursing and Health Sciences

Florida International University

In partial fulfillment of the requirements
For the Degree of Doctor of Nursing Practice

By

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ABSTRACT

Background: The incidence of postoperative nausea and vomiting (PONV) following general anesthesia remains high despite the increasing number of healthcare advances. Aprepitant has demonstrated promising effectiveness in the prevention of PONV and can add value to current healthcare practices. Further investigation is needed to determine aprepitant's effectiveness and best use to create practice recommendations.

Objectives: (1) To evaluate the effectiveness of aprepitant versus ondansetron in the prevention of PONV utilizing three databases: PubMed, CINAHL, and EMBASE. This systematic review will serve as the basis for objective two. (2) To demonstrate an increase in knowledge of anesthesia providers pertaining to the use of aprepitant in the prevention of PONV.

Methodology: Ten articles, including eight randomized controlled trials (RCTs) and two systematic reviews, were deemed eligible for use in this systematic review. Based on the evidence from these ten articles, aprepitant was found to have superior protection against PONV in comparison to ondansetron; aprepitant in combination with ondansetron was shown to have more effectiveness than ondansetron alone against PONV; and aprepitant demonstrated improved effectiveness in the prevention of postoperative vomiting and time to first vomiting episode. With this information, a pre-test, educational module, and post-test were created for anesthesia providers to evaluate baseline knowledge and knowledge growth.

Results: The statistical analysis between the pre-test and post-test demonstrated an increase in provider knowledge on PONV and use of aprepitant.

Conclusions: Aprepitant administered alone along with aprepitant administered with ondansetron is more effective than ondansetron alone in reducing PONV rates. Implementation of an educational based intervention increased providers knowledge on information pertaining to aprepitant and its use in the prevention of PONV. Continual implementation of this quality improvement project has the potential to lead to decreased PONV rates, improved patient outcomes, and increased patient satisfaction.

Keywords: Aprepitant, Antiemetic, Ondansetron, Nausea, Vomiting, Postoperative nausea and vomiting (PONV)

INTRODUCTION

Description of the Problem

The National Library of Medicine defines postoperative nausea and vomiting (PONV) as nausea and/or vomiting that occurs immediately in the first 24 hours after surgery.¹ PONV, along with pain, is one of two of the most common patient complaints reported after surgery and is the leading cause of unplanned inpatient admissions.¹ There have been various guidelines published from different societies regarding pharmacological and nonpharmacological treatments to prevent PONV, yet PONV rates remain high.¹ PONV rates remain high despite improvements in healthcare, including the availability of multiple prophylactic antiemetic agents, the use of minimally invasive surgical techniques, and the availability of short-acting anesthetics.² The incidence rates for inpatient surgeries range between 30% to 50%, with rates as high as 70% to 80% for patients with multiple risk factors.³ It has been argued that the continued high incidence is related to the increasing number of ambulatory surgeries and the increased emphasis on earlier mobilization and discharge.²

In the United States, more than 40 million people each year will undergo surgery.⁴ At least 30% of those people will experience PONV if no intervention is instituted.⁴ Even patients with no known risk factors still have a 10% chance of developing PONV after surgery.⁴ Effects of PONV can range anywhere from postoperative patient dissatisfaction or distress to postoperative morbidity.⁴ Patient dissatisfaction with anesthesia seems to be a glaring negative consequence of PONV. In one study of surgical patients, patients reported nausea and vomiting as 2 of the top 3 most concerning possible anesthesia outcomes, along with pain.¹ Vomiting was rated as number 1, followed by pain at number 2, and nausea at number 3.¹ Patients have also reported that they were willing to pay up to \$100 out of pocket for medications that would prevent PONV.³ Unfortunately, patient dissatisfaction is not the only consequence of ignoring this problem. PONV has been implicated as the cause of delayed PACU discharge, resulting in up to twice the time in PACU than patients who did not experience symptoms.³ Not only is this a problem for

patients but for the efficiency of patient flow from the operating room to PACU.³ Disruption of patient flow can result in increased healthcare spending.³ Additionally, PONV can produce patient complications, including pulmonary aspiration, wound dehiscence, esophageal rupture, subcutaneous emphysema, pneumothorax, and more.³

It is evident that PONV remains a current problem in anesthesia. Extensive research has contributed to improvements in PONV, yet there is still no established antiemetic regimen.² More comprehensive research needs to be completed regarding the most effective prophylactic regimen. Failure to address this problem will result in continued patient dissatisfaction with anesthesia, lengthened post-anesthesia recovery unit (PACU) stays, and increased healthcare costs, among other things.³

Background and significance

The pathogenesis of nausea and vomiting is extremely complex, making treatment and prevention much more challenging despite the abundance of published studies.⁵ The mechanism of vomiting can result from stimulation of five different afferent pathways: the chemoreceptor trigger zone, vagal stimulation via the gastrointestinal system, neuronal activation of the vestibular system, reflex afferent pathways from the cerebral cortex, and afferent pathways from the midbrain.⁵ Input from any one of these pathways to the vomiting center, located in the medulla oblongata, will result in the vomiting reflex via agonism or antagonism of a variety of different receptors.¹ Therefore, many drugs can be used as a multimodal treatment for nausea and vomiting. However, PONV has been proven to be much more challenging to treat once it ensues.¹

Prevention has been recognized as the best method for decreasing PONV's incidence.¹ Therefore, identification of high-risk patients and knowledge of associated risk factors are pivotal to reducing rates. A preoperative risk assessment tool used to identify high-risk patients is the Apfel scoring system, which is based on four independent risk factors.⁵ These include female gender, non-smoking status, history of PONV and/or motion sickness, and use of postoperative opioids.⁶ Of these four risk factors, female gender has the most significant influence on the

incidence of PONV, with females being three times more likely than males to develop PONV.⁶ For this reason, the female population, requires a more calculated and comprehensive approach to PONV prophylaxis. According to the Apfel scoring system, female gender alone places patients at a 20% risk for developing PONV.⁶ Each additional risk factor on the scoring system increases patients' risk by 20%.⁶ For example, patients with an Apfel score of 4 have an 80% chance of developing PONV without any intervention.⁶

Other risk factors for PONV include surgical procedure, anesthetic drug of choice, and duration of surgery.^{1,5} For example, laparoscopic and gynecological surgeries tend to have a higher incidence of PONV.⁵ Surgeries lasting longer than 30 minutes may increase the risk of PONV by up to 60%.⁵ Additionally, specific anesthetic agents such as nitrous oxide and volatile anesthetics increase PONV risk.⁵ Some modifiable risk factors that can be adjusted to decrease the risk of PONV for a selected patient could include the anesthetic of choice or the use of antiemetic agents.³ However, many risk factors are nonmodifiable, such as female gender and surgical procedure.³ For example, the anesthesia provider may choose a total intravenous approach (TIVA) over inhaled anesthetics. However, the patient may still be a young female with a history of PONV presenting for a gynecological surgery. All of these circumstances place the patient at high risk for PONV.³ Therefore, an effective prophylactic regimen must be established. Anesthesia providers must be able to identify patients with nonmodifiable risk factors and treat them appropriately. It is important to note that the American Society of Anesthesiologists recommends PONV prophylaxis only when risk factors exist.¹ Many of the antiemetics in practice accompany undesirable side effects where risks for PONV prevention outweigh the benefits.¹

There are a large number of antiemetic drugs approved for treatment and prevention of PONV, which include 5-hydroxytryptamine (5-HT₃) receptor antagonists, corticosteroids, butyrophenones, neurokinin-1 (NK-1) receptor antagonists, etc.² Nonetheless, patients given antiemetics such as the commonly used 5-HT₃ antagonist, ondansetron, still experience PONV

30% to 40% of the time.⁷ Multiple studies have shown that combination therapy with antiemetic agents from different drug classes is more effective than single-agent antiemetic treatment.⁸

Consensus guidelines published by the American Society of Anesthesiologists (ASA) in January of 2014 set forth eight different recommendations for the management of postoperative nausea and vomiting.⁹ The ASA recommends (1) identification of patients' at risk for PONV (2) reduction of baseline patient risk factors for PONV (3) administration of PONV prophylaxis with 1 to 2 interventions for adults at moderate risk (4) administration of 2 or greater interventions for patients at high risk for PONV (5) administration of prophylactic therapy to children at increased risk for postoperative vomiting (6) administration of antiemetic agents to patients with PONV who did not receive prophylaxis or in with whom prophylaxis failed (7) institution of PONV prevention treatment in the clinical setting and (8) use of general multimodal prevention to streamline implementation of PONV policies.⁹ While these guidelines may help guide anesthesia providers in preventing PONV, they do not provide specific instructions on which antiemetic agent is most efficacious for a given patient population.

Systematic Review Rationale

There has been minimal use of the class of antiemetics drugs known as neurokinin-1 (NK-1) antagonists despite their promising effectiveness.⁷ NK-1 antagonists are a relatively new class of antiemetics used to prevent nausea and vomiting.⁷ One drug in this class, aprepitant, has been approved and shown to be effective for the treatment of chemotherapy-induced nausea and vomiting when used in combination with other antiemetics.⁷ Recently, more studies have been conducted regarding its effectiveness in the treatment and prevention of postoperative nausea and vomiting.

Aprepitant works primarily in the nucleus tractus solitarius as well as in areas of the reticular formation by antagonizing NK-1 receptors to exert its antiemetic effects.⁵ One particular point of interest in antagonism of the NK-1 receptor is its ability to block the effects of the substrate substance P.⁸ Substance P is the most abundant neurokinin found in the central and

peripheral nervous system.⁸ It is released in response to input from the gut and the brain, leading to activation of NK-1 receptors, resulting in the vomiting reflex.⁸ Activation of NK-1 receptors in response to up-regulation of receptors in cortical neurons is also thought to be the cause of opioid-induced nausea and vomiting.¹⁰ Therefore, it is reasonable to consider that aprepitant may effectively prevent nausea and vomiting associated with opioid administration.¹⁰

Aprepitant is recommended for administration 3 hours or less before induction of anesthesia at a dose of 40 mg PO for PONV prophylaxis.⁴ A unique characteristic of aprepitant is its particularly long half-life of 40 hours, unlike most antiemetics.⁹ In two large randomized controlled trials, aprepitant has displayed similar effectiveness to the commonly administered 5HT-3 antagonist, ondansetron, in the prevention of vomiting and use of rescue antiemetics within the first 24 hours after surgery.⁹ However, aprepitant was shown to be noticeably more effective in reduction of nausea and vomiting at 24 and 48 hours post-surgery.⁹ Aprepitant has also displayed greater antiemetic efficacy in comparison to ondansetron.⁹

While some studies have proven the promising nature of aprepitant's antiemetic effects and use in the prevention of PONV, more studies need to be conducted to fully establish its effectiveness and best use.⁹ Further information is needed regarding the most effective use for routine prophylaxis, the patient population that would benefit most from aprepitant's administration, and for which medications that it may show an additive or synergistic relationship.⁹ It has been argued that aprepitant should be administered for PONV prophylaxis specifically in patients at risk for PONV with whom vomiting could result in serious complications, and in patients in which concerns for adverse side effects exist regarding administration of less costly antiemetics, such as ondansetron.²

Objectives of the Systematic Review

The purpose of this systematic review is to locate all current evidence on the efficacy of aprepitant in comparison to ondansetron for postoperative nausea and vomiting. Each chosen study will be analyzed for significant findings related to aprepitant's effectiveness compared to

the antiemetic ondansetron in the prevention of PONV, specifically in patients 18 years or older. This systematic review answered the PICO question: “(P) In patients 18 years or older undergoing general anesthesia, (I) does the administration of aprepitant, including the combination of aprepitant with ondansetron, (C) compared to ondansetron alone (O) reduce incidence rates of PONV?”

METHODOLOGY

Databases and Search Strategy

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used to conduct the search for this review.¹¹ The formatting of this paper was also accomplished in accordance with PRISMA guidelines.¹¹ The three databases used to complete the search for this review were PUBMED, Excerpta Medica Database (EMBASE), and Cumulated Index to Nursing and Allied Health Literature (CINAHL). The included search terms were selected based on the chosen PICO question. Search terms used in also three searches include “aprepitant,” “comparison,” “ondansetron OR zofran,” and “PONV.” Additional terms included in the search strategy for each concept or topic were added to ensure all relevant studies were identified. The excluded terms were selected based on a large number of irrelevant results associated with those terms. PUBMED yielded a total of 109 results, EMBASE yielded a total of 76 results, and CINAHL yielded a total of 8 results. Table 1 below contains all detailed information regarding the conducted search strategy, including exact included search terms, excluded search terms, applied filters, and the number of results.

Table 1. Database Search Table

Concepts/ Topics	Aprepitant or Emend	Comparison	Ondansetron or Zofran	Postoperative Nausea and Vomiting	Filters Applied
PUBMED	aprepitant OR emend OR "NK-1 antagonist*" OR "Neurokinin	comparison OR comparing OR versus	ondansetron OR zofran OR "serotonin 5-HT3 antagonist*" OR "5-HT3 antagonist*"	"postoperative nausea and vomiting" OR "ponv" OR "post operative nausea and	125 results Filter applied: publication date between

	1 receptor antagonist*" OR "Neurokinin 1 antagonist"			vomiting" OR "nausea and vomiting"	2007-2020. Resulted in 109 results total.
CINAHL	aprepitant OR emend OR "NK-1 antagonist*" OR "Neurokinin 1 receptor antagonist*" OR "Neurokinin 1 antagonist"	comparison OR comparing OR versus	ondansetron OR zofran OR "serotonin 5-HT3 antagonist*" OR "5-HT3 antagonist*"	"postoperative nausea and vomiting" OR "ponv" OR "post operative nausea and vomiting" OR "nausea and vomiting" NOT chemotherapy	9 results Filter applied: publication dates between 2007-2020. Resulted in 8 results total.
EMBASE	aprepitant OR emend OR "NK-1 antagonist*" OR "Neurokinin 1 receptor antagonist*" OR "Neurokinin 1 antagonist"	comparison OR comparing OR versus	ondansetron OR zofran OR "serotonin 5-HT3 antagonist*" OR "5-HT3 antagonist*"	"postoperative nausea and vomiting" OR "ponv" OR "post operative nausea and vomiting" OR "nausea and vomiting" NOT chemotherapy	“Quick search” used in all fields to get 96 results found Filters applied: Publication dates between 2007-2020. Resulted in 76 total results.

Study Selection and Screening Method

The program Endnote was utilized for screening, study selection, and organization of articles. Search results were first imported separately from each database into Endnote. A group was then created with all 193 articles from the 3 separate databases. Duplicates were then located using the “Find Duplicates” option in Endnote, which identified a total of 31 duplicate articles. After the duplicates were removed, a total of 162 articles were left to be screened and assessed for eligibility in this review. New folders were created for organizational placement during the screening process with titles “Background,” “Applicable,” and “Not applicable.” During the

screening process, the investigator reviewed all articles titles and abstracts, and placed each article in the appropriate folder based on that information. Articles that were clearly unrelated to the PICO question were placed in the “Not applicable” folder. Articles that were related to the PICO but needed further review for selection were placed in the “Applicable” folder. Those that were relevant to the PICO but were not actual studies were placed in the “Background” folder. The “Not applicable” folder ended up with 111 articles that were excluded in the screening process, leaving a total of 51 articles for further review.

A full-text screening process was completed by the investigator on all 51 “Applicable” articles based on strict inclusion and exclusion criteria. A detailed list of the inclusion and exclusion criteria is displayed in Table 2. Articles that met inclusion criteria included those with a patient population aged 18 years or older, those that compared a single dose of aprepitant or aprepitant with ondansetron to ondansetron alone, and those that measured PONV and use of rescue antiemetics as the outcome. Additional inclusion criteria included publications in the English language between the dates of 2007 and 2020. Randomized controlled trials (RCTs), systematic reviews, and meta-analyses were utilized to complete this review. Exclusion criteria included patients less than 18 years of age, patients receiving chemotherapy, or patients receiving medications that are known to cause nausea and/or vomiting. Studies that were excluded were those that involved use of any other antiemetic combination therapy other than ondansetron with aprepitant for PONV prophylaxis or that studied aprepitant versus ondansetron for use in prevention of chemotherapy induced nausea and vomiting.

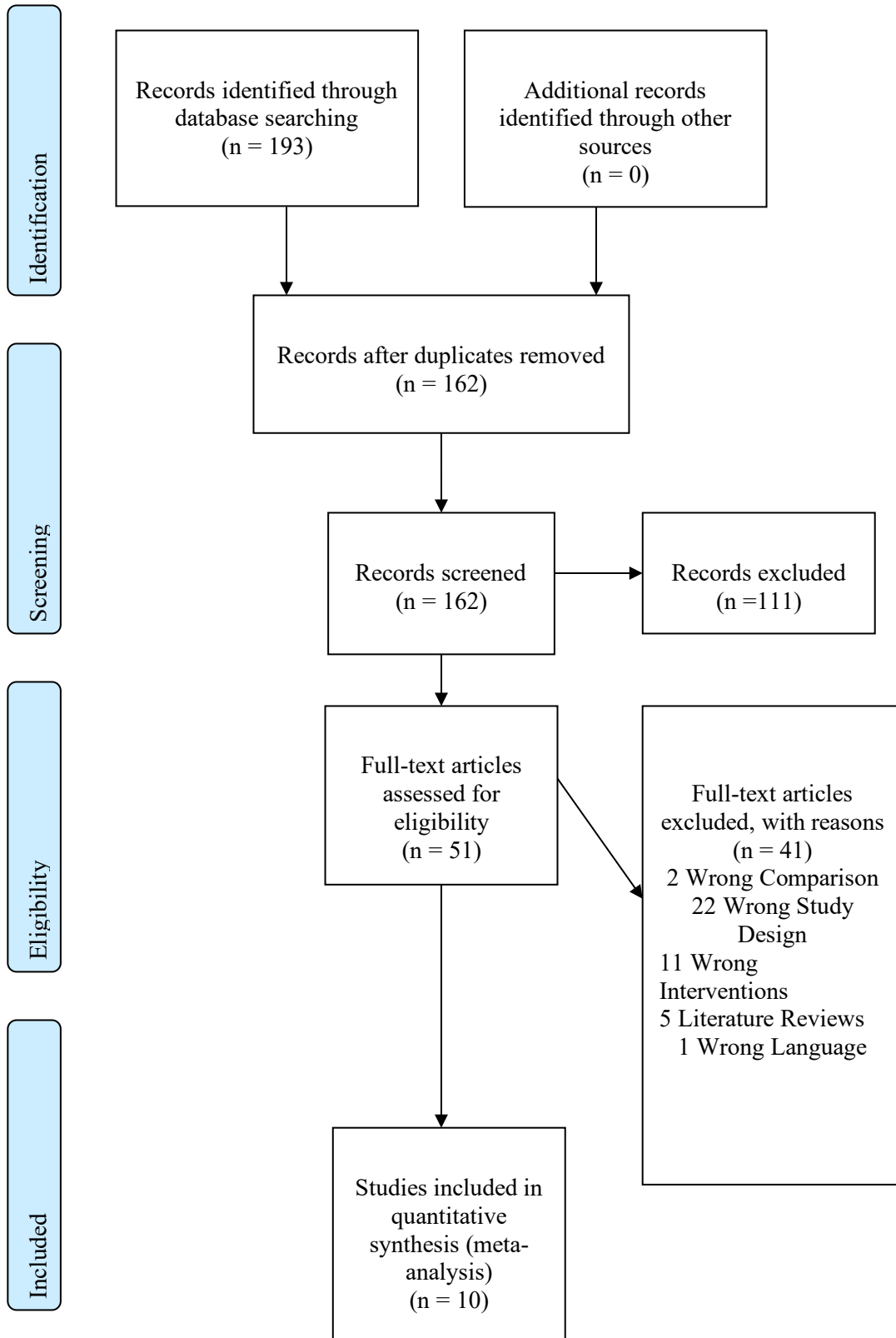
Several studies were excluded because of additional antiemetic agents in conjunction with aprepitant or ondansetron as the intervention. If any other antiemetic agents were given in the intervention or comparison, they were excluded to eliminate inaccurate findings, with the exception of ondansetron with aprepitant as the intervention. A number of studies were also excluded because chemotherapy or radiation therapy induced nausea and vomiting was studied, rather than postoperative nausea and vomiting. A total of 193 articles were identified between the

three databases. After duplicates were removed, 162 articles were screened and assessed for eligibility. The screening process identified 111 articles for exclusion based on information given in the article's title and abstract. Another 41 articles were excluded as they did not fit the chosen PICO question. This left a total of 10 studies relevant to the PICO question to be included in this review. A PRISMA flow diagram is provided in Figure 1, which displays the full process for study selection.

Table 2. Inclusion & Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Population <ul style="list-style-type: none"> • Age > or = 18 years of age • Males & Females 	Population <ul style="list-style-type: none"> • Age < 18 years of age • Patients receiving chemotherapy • Patients taking medications that are known to cause nausea and/or vomiting
Intervention <ul style="list-style-type: none"> • Single dose aprepitant for PONV prophylaxis • Aprepitant + ondansetron • General Anesthesia 	Intervention <ul style="list-style-type: none"> • Aprepitant + any other antiemetic other than ondansetron for PONV prophylaxis (i.e., Aprepitant + decadron, Aprepitant + scopolamine) • Aprepitant vs ondansetron for chemotherapy induced nausea and vomiting • Regional Anesthesia only
Comparison <ul style="list-style-type: none"> • Ondansetron alone for PONV prophylaxis 	Comparison <ul style="list-style-type: none"> • Decadron or any other antiemetic • Total intravenous anesthesia (TIVA) • No antiemetic
Outcome <ul style="list-style-type: none"> • Rates of PONV • Need for rescue antiemetics postoperatively 	Outcome <ul style="list-style-type: none"> • Anything other than PONV or need for rescue antiemetics
Type of study <ul style="list-style-type: none"> • Published between 2007-2020 • Randomized Controlled Trials • Systematic Reviews • Meta Analyses • English language 	Type of study <ul style="list-style-type: none"> • Published before 2007 • Dissertation/theses • Surveys • Expert Opinions • Non-English language

Figure 1. PRISMA Flow Diagram



Collection, Analysis, & Data Items

The ten identified relevant studies were appraised utilizing John's Hopkin's research evidence appraisal tool.¹² This tool helped to rate each study based on its level of evidence and quality.¹² Evidence level was rated from I to IV, with level I evidence being the highest level of evidence and level IV being the lowest level of evidence.¹² Level I studies include any experimental studies, randomized controlled trials (RCTs), systematic reviews of RCTs, or meta-analyses.¹² Level II studies include quasi-experimental studies and systematic reviews of quasi-experimental studies with or without meta-analyses.¹² Level III studies are non-experimental studies, any systematic reviews including non-experimental studies, or qualitative studies.¹² Level IV studies include expert opinions including opinions of recognized and respected authorities or organizations.¹² This includes expert committees that develop recommendations based on scientific evidence including clinical practice guidelines and consensus panels.¹¹

Each study was rated as high quality, good quality, or low quality with major flaws utilizing John's Hopkin's research evidence appraisal tool.¹² A high-quality rating was given to studies that have an appropriate sample size, proper control, generalizable results, and recommendations that are consistent with the current literature.¹² Studies were rated as good quality in the presence of generally consistent results, a reasonable sample size, some control, and fairly consistent findings and recommendations based on a comprehensive literature review.¹² Those considered low quality or with major flaws were those with little evidence or inconsistencies, those with an inadequate sample size, and those in which conclusions could not be drawn from the study.¹²

The ten studies included in this review included 1 post hoc analysis of two randomized controlled trials, 5 randomized double blind controlled trials, 2 randomized controlled trials, and 2 systematic review and meta-analyses. All studies included are experimental studies as they include an intervention, control, randomization, and manipulation of at least 1 variable.¹² All studies were also classified as Level I evidence based on John's Hopkins research evidence

appraisal tool.¹² Questions that were used to come to this determination for the post hoc analysis and RCTs included, “Was there manipulation of an independent variable?,” “Was there a control group?,” “Were study participants randomly assigned to the intervention and control groups?”¹² Each study included in both systematic review and meta-analyses was an RCT, making them both a Level I evidence study.¹² In order to determine the quality of evidence for the RCTs, the investigator reviewed the article to determine if (1) the problem was clearly identified (2) the purpose of the study was clearly stated (3) the literature review was current within the last 5 years (4) the sample size was sufficient (5) the data collection methods were clearly described (6) reliability and validity were assessed and discussed (7) the results were presented clearly (8) the limitations were discussed and (9) conclusions were based on the results.¹²

To determine the quality of evidence for the systematic reviews, the investigator reviewed the article to determine if (1) the variables of interest were clearly identified (2) the search was comprehensive and reproducible with mention of multiple search databases, terms, and inclusion/exclusion criteria (3) there was a flow diagram with a breakdown of the screening and review process (4) all details included in the studies were presented (5) methods for appraisal were described (5) conclusions were based on results and (6) limitations were discussed.¹² Table 3 below provides a breakdown of the level and quality of evidence for each study included in this review based on the above mentioned criteria.

Table 3. Study characteristics

Author & Year	Type of study, Level and Quality of Evidence	Participants, Surgical Procedure, & Setting	Intervention & Comparison
Diemunsch P, Apfel C, Gan TJ, et al., 2007.	Post hoc analysis of pooled data from two RCTs, Level I, Good quality	1599 patients age 18 years or older, ASA I-III, 92% female population, Mean age=46, open abdominal surgery requiring overnight stay, 82% were gynecological	Aprepitant 40 mg PO vs Aprepitant 125 mg PO vs Ondansetron 4 mg IV

		surgery, 18% were non-gynecological surgery	
Diemunsch P, Gan TG, Philip BK, et al., 2007.	Randomized double-blind controlled trial, Level I, High quality	992 patients age 18 years or older, ASA I-III, open abdominal surgery, 42 centres included (8 U.S. sites and 34 non-U.S. sites in North America, South America, Europe, Australia, and Asia)	Aprepitant 40 mg PO vs Aprepitant 125 mg PO vs Ondansetron 4 mg IV
Gan TJ, Apfel CC, Kovac A, et al., 2007.	Randomized double-blind controlled trial, Level I, High quality	805 patients age 18 years or older, ASA I-III, abdominal surgery, 29 centers	Aprepitant 40 mg PO vs Aprepitant 125 mg PO vs Ondansetron 4 mg IV
Ham SY, Shim YH, Son MJ, et al., 2016	Randomised controlled trial, Level I, High quality	125 female patients age 22-55 years old, ASA I & II, gynecological laparoscopic surgery, single-center in Korea	Aprepitant 80 mg PO + Ondansetron 4 mg IV vs Ondansetron 4mg IV alone
Jeyabalan S, Thampi SM, Karuppusami R, Samuel K., 2019.	Double blinded, randomised controlled trial, Level I, High quality	125 female patients Age 18 -65 years, ASA I-II, breast and thyroid surgeries, tertiary care hospital	Aprepitant 40 mg PO alone vs Ondansetron 8 mg alone
Lim CS, Ko YH, Park SI, et al., 2013.	Randomized controlled trial, Level I, Good quality	90 patients, age 18-65 years old, ASA I-II, Rhinolaryngological surgery	Aprepitant 80 mg + Ondansetron 4 mg vs Aprepitant 125 mg + Ondansetron 4 mg vs Ondansetron 4 mg alone
Liu M, Zhang H, Du B, et al., 2015.	Systematic Review and Meta-analysis, Level I, High quality	Sample size varies by study, age 18 years or older, ASA I-III, variety of surgical procedures, 5 multicenter studies, 9 single-centered studies	Ondansetron vs aprepitant alone, & aprepitant + ondansetron vs ondansetron alone
Singh PM, Borle A, Rewari V, et al., 2016	Systematic Review and Meta-analysis, Level I, High quality	Sample size varies by study, age 18 years or greater undergoing elective surgery, single and multicenter studies	Ondansetron vs aprepitant alone, & aprepitant + ondansetron vs ondansetron alone
Sinha AC, Singh PM, Williams NW, et al., 2014.	Double-blind placebo-controlled trial,	125 morbidly obese patients, ASA I to III patients aged 18 years	Aprepitant 80 mg + Ondansetron 4mg vs

	Level I, High quality	or older, patients at high risk for PONV, bariatric surgery, Hospital of the University of Pennsylvania in Philadelphia	Placebo + Ondansetron 4 mg
Vallejo MC, Phelps AL, Ibinson JW, et al., 2012.	Prospective, double-blinded, randomized, two-arm evaluation study Level I, Good quality	150 patients undergoing outpatient plastic surgery, males and females age 18-65 years old	Aprepitant + Ondansetron vs Placebo + Ondansetron

RESULTS

Study selection

As portrayed in the PRISMA diagram in Figure I, a total of 193 articles were identified during the initial search process. After the screening process was completed, a total of ten articles were selected to be included in this review based on strict inclusion criteria. Each of these articles answers the chosen PICO question: “In patients 18 years or older undergoing general anesthesia, does the administration of aprepitant, including the combination administration of aprepitant with ondansetron, compared to ondansetron alone, reduce incidence rates of PONV?” The two systematic reviews included in this review evaluate both aprepitant with zofran and aprepitant administration alone with ondansetron alone as the comparison. These articles also include other combinations of aprepitant that are not included in answering the mentioned PICO question. Four out of the ten selected articles measure aprepitant alone versus ondansetron alone, and the other four studies measure combination therapy of ondansetron with aprepitant versus ondansetron alone. The four studies that measure combination therapy with aprepitant and ondansetron were also included in this review based on recommendations from the ASA guidelines discussed earlier that recommend combination therapy for patients at high risk.⁹ Table 3 above lists each study selected to be included in this systematic review, along with level of evidence, population, settings, intervention, and comparison.

Study characteristics

The eight randomized controlled trials that were included in this review had a total of 4,011 patients who received either aprepitant alone, aprepitant with ondansetron, or ondansetron alone. Diemunsch et al, Diemunsch et al, and Gan et al contributed the most patients to this review with 1599, 992, and 805 patients respectively.^{13,7,9} Patients in the studies conducted by Diemunsch et al, Diemunsch et al, Gan et al, and Jeyabalan et al received either a dose of aprepitant alone or a dose of ondansetron alone.^{13,7,9,14} This included 3,521 total patients. The remaining 490 patients from RCT studies conducted by Ham et al, Lim et al, Sinha et al, and Vallejo et al. received either aprepitant in combination with ondansetron or ondansetron alone.^{15,16,17,18} All studies were published between 2007 and 2019 in the English language. Surgical procedures included open abdominal, laparoscopic gynecological, rhinolaryngeal, outpatient plastic, breast, thyroid, and bariatric surgeries. One study by Ham et al studied the efficacy of aprepitant with ondansetron versus ondansetron alone in patients who underwent laparoscopic gynaecological surgery on a postoperative fentanyl-based patient-controlled analgesia (PCA) pump with 12 mg of added ondansetron to the PCA solution.¹⁵

Patient and hospital demographics. Both male and female patients were included as part of this review. All studies included both female and male patients with the exception of Ham et al and Jeyabalan et al, which only included female patients.^{15,14} Patients ranged from ASA class I to ASA class III, and all patients were age 18 years or older. One study by Sinha et al studied morbidly obese patients with a body mass index (BMI) > 40 kg/m³ who were considered at high risk for PONV.¹⁷ The RCTs were conducted across the world including the United States, North America, South America, Asia, Europe, Australia, and Korea. Most studies were conducted in a hospital setting with the exception of Vallejo et al that conducted the study in an outpatient plastic surgery center.¹⁸

Methodology. As previously mentioned, patients in all 8 RCTs either studied aprepitant alone versus ondansetron alone, or aprepitant in combination with ondansetron versus

ondansetron alone. The dose of aprepitant varied throughout some of the studies. Four RCTs measured aprepitant versus ondansetron alone, and the other four RCTs measured aprepitant in combination with ondansetron versus ondansetron alone. Of the RCTs measuring aprepitant versus ondansetron alone, three studies measured the same doses of aprepitant and ondansetron at the same time.^{13,7,9} Diemunsch et al, Diemunsch et al, and Gan et al all randomly assigned patients via computer randomization to receive preoperative doses of (1) aprepitant 40 mg PO (2) aprepitant 125 mg PO or (3) ondansetron 4 g IV.^{13,7,9} In all three of these studies, either aprepitant or placebo was given 1–3 hours before induction of anesthesia, along with administration of either intravenous ondansetron or placebo given over 2–5 minutes immediately prior to induction of anesthesia.^{13,7,9} The fourth RCT that measured aprepitant versus ondansetron alone was by Jeyabalan et al, which measured only 1 dose of aprepitant PO.¹⁴ Jeyabalan et al randomly assignment patients to two groups to either receive aprepitant 40 mg PO preoperatively or placebo, and injection of ondansetron 8mg IV or placebo IV before the end of surgery and again for two more doses, 8 hours apart.¹⁴

The other four RCTs that measured aprepitant as combination therapy with ondansetron in comparison to ondansetron alone include Ham et al, Lim et al, Sinha et al, and Vallejo et al.^{15,16,17,18} All RCTs administered aprepitant 80 mg prior to induction of anesthesia, with the exception of Vallejo et al that administered 40 mg of aprepitant prior to induction.^{15,16,17,18} Each of these RCTs comparing combination therapy of aprepitant and ondansetron versus ondansetron alone administered one dose of ondansetron at 4 mg, with the exception of Ham et al.^{15,16,17,18} Ham et al administered ondansetron 4 mg IV at the end of surgery, and also added 12 mg of ondansetron the fentanyl based PCA solution that was to be infused in the postoperative period.¹⁵ Aprepitant was administered preoperatively in all four RCTs. However, the timing of ondansetron was different in one of the studies. Lim et al, Ham et al, and Sinha et al all administered ondansetron just prior to the end of surgery, whereas Vallejo et al administered ondansetron immediately after induction of anesthesia.^{15,16,17,18}

All RCTs included in this review assessed nausea scores for 48 hours postoperatively, except for Sinha et al that assessed nausea scores for 72 hours postoperatively and Jeyabalan et al that assessed nausea scores for only 24 hours after surgery.^{7,9,13,14,15,16,17,18} However, nausea scores were evaluated using different scales, by different methods, and at different time intervals.

Diemunsch et al, Diemunsch et al, Gan et al, and Jeyabalan et al measured nausea scores using the Verbal Rating Score (VRS), which measures nausea on a scale from '0' to '10' where '0' is 'no nausea' and 10 is 'nausea as bad as it could be.'^{7,9,13,14} Sinha et al and Vallejo et al also used the VRS scoring system; however, Sinha et al defined a score of '10' as 'worst possible urge to vomit' and Vallejo et al defined a score of '10' as 'worst possible nausea ever.'^{17,18} Diemunsch et al, Diemunsch et al, and Gan et al assessed patients nausea scores at hours 2, 4, 6, 24 and 48 after surgery, at any point during the postoperative period that the patient complained of nausea, and before administration of rescue therapy if needed.^{7,9,13} Jeyabalan et al assessed patients' nausea scores with the VRS scoring system at three different points in the postoperative period: (1) 0-2 hours (2) 2-12 hours and (3) 12-24 hours.¹⁴ Sinha et al assessed patients nausea scores 30 minutes, 1 hour, 2 hours, 6 hours, 24 hours, 48 hours, and 72 hours postoperatively.¹⁷

Vallejo et al measured nausea scores using the VRS scoring system on admission to PACU and every hour until the patient was discharged.¹⁸ Since the patients used in this study underwent outpatient surgery, each patient was sent home with a diary to be filled out.¹⁸ This diary required patients to record a nausea score and whether they retched or vomited every four hours while awake for the first 24 hours, and every 8 hours while awake from 24 to 48 hours postoperatively.¹⁸ Data from these diaries was obtained via a telephone survey from a follow up with the primary investigator.¹⁸ Ham et al utilized the Verbal Numerical Rating Score (VNRS) to measure the intensity of nausea from '0' to '10' with '0' as 'no nausea' and '10' as the 'worst nausea imaginable.'¹⁵ VNRS scores were assessed during 4 different intervals: (1) 10 minutes after arrival to the PACU (2) upon PACU discharge to 6 hours postoperatively (3) between 6 to 24 hours postoperatively and (4) between 24 to 48 hours postoperatively.¹⁵ These scores were

record by a nurse blinded to the study.¹⁵ Lastly, Lim et al utilized the Rhodes Index of Nausea, Vomiting, and Retching (RINVR) scoring system to assess patients' nausea scores postoperatively.¹⁶ RINVR scores were assessed at 6 hours and 24 hours in the postoperative period.¹⁶ This nausea assessment is based on 8 different questions.¹⁶ Based on the response to each question, a score of 0-4 points is given, with a total possible score of 32.¹⁶ A score of 0 signifies no distress or nausea, whereas a score of 32 signifies severe distress or nausea.¹⁶

Definitions and Findings of Outcomes

The main variables that were measured throughout the studies were severity of nausea, retching or vomiting, and use of rescue antiemetics. The severity of nausea was measured using either the Verbal Rating Score (VRS), the Verbal Numeric Rating Score (VNRS), or the Rhodes Index of Nausea, Vomiting, and Retching (RINVR) scoring system.^{7,9,13,14,15,16,17,18} The RCTs had similar definitions of nausea, retching, vomiting, and an emetic episode. Gan et al defined an emetic episode as “one or more continuous episode of vomiting (oral expulsion of stomach contents) or retching (an attempt to vomit that is not productive of stomach contents); distinct episodes were those occurring at least 1 min apart.”⁹ Jeyabalan et al defined an emetic episode as “a single retch or vomit or any number of continuous vomits or retches.”¹⁴ Jeyabalan also defined retching as “an effort to vomit which is not under voluntary control and that does not cause expulsion of stomach contents” and vomiting as “an expulsion of stomach contents.”¹⁴ Sinha et al defined retching as “expulsive attempts without any oral content” and vomiting as “as oral expulsion of gastric contents.”¹⁷ Additionally, Sinha et al defined an emetic episode as “any episode of vomiting or retching.”¹⁷

Most studies involved in this review found aprepitant alone to be superior to ondansetron alone in prevention of postoperative nausea and vomiting. Studies that measured aprepitant as combination therapy with ondansetron in comparison to ondansetron alone all found combination therapy with aprepitant to be more efficacious than ondansetron alone.^{15,16,17,18} Both studies by Diemunsch et al found aprepitant to be superior to ondansetron in both postoperative nausea and

vomiting, whereas Gan et al found aprepitant superior only in the prevention of postoperative vomiting.^{7,9,13} Diemunsch et al found that administration of aprepitant at doses of 40 mg and 125 mg provided superior protection against nausea, vomiting, and need for rescue antiemetics in comparison to ondansetron 4 mg IV.¹³ Overall, patients that were given aprepitant preoperatively had lower nausea scores than those who received ondansetron alone.¹³ Diemunsch et al found that patients who received aprepitant were twice as likely to be protected against vomiting episodes in comparison to those that only received ondansetron.⁷ Additionally, time to first vomiting episode was delayed in those who received aprepitant.⁷ The dose of aprepitant administered seemed to have no statistically significant difference in the efficacy of prevention of nausea and vomiting.⁷ Therefore, it was concluded that a dose of 40 mg of aprepitant is sufficient for PONV prophylaxis.⁷ The last RCT that was included in this review that studied ondansetron alone versus aprepitant alone was Jeyabalan et al, which actually found ondansetron and aprepitant to have the similar efficaciousness in prevention of PONV.¹⁴ There was no significant difference in prevention of emetic episodes, incidence of nausea, or time to request of rescue antiemetic.¹⁴ However, Jeyabalan et al did find that the aprepitant group took longer to develop the first episode of vomiting and to receive the first dose of rescue antiemetics.¹⁴

All four RCTs that measured the combination administration of aprepitant with ondansetron in comparison to ondansetron alone found that the addition of aprepitant to ondansetron was superior to that of ondansetron alone in preventing of PONV.^{15,16,17,18} Ham et al and Sinha et al both found that the time to first vomiting was prolonged in the patients who received aprepitant with ondansetron.^{15,17} According to Sinha et al, nausea scores generally peak at 4 hours after emergence from anesthesia.¹⁷ However, the group that received aprepitant had no episodes of vomiting during this time period, and up until 6 hours postoperatively, supporting the hypothesis that aprepitant delays time to first vomiting.¹⁷

Recommendations and Limitations

Limitations existed across the RCTs included in this systematic review that could have altered nausea scores, vomiting episodes, and use of rescue antiemetics. This could have altered results and findings from these studies. A few limitations that existed throughout the majority of the RCTs were that the timing of ondansetron administration and use of rescue antiemetics could have had a large impact on the severity of nausea, and the subjectiveness of nausea could have altered results. Jeyabalan et al mentioned that a major limitation to the study was that aprepitant was administered at a dose of 40 mg, yet previous studies have found that aprepitant is more efficacious at higher doses of 80 mg and 125 mg.¹⁴ Therefore, this could have influenced nausea scores. The study conducted by Lim et al stated that a limitation to the study was that patients included in the study did not have a large number of risk factors for PONV, which could have resulted in patients having low incidences of nausea and vomiting.¹⁶ Sinha et al mentioned that opioid consumption was not compared between the two groups, which could have had an effect on nausea.¹⁷ Vallejo et al mentioned two limitations: (1) patients who required rescue therapy received standardized treatment based on the institutions protocol for PONV, which may have affected the patients' outcomes and (2) ondansetron was administered on induction to ensure that all patients would receive the medication since the duration of the surgeries varied. Most research states that ondansetron has improved efficacy just prior to emergence.¹⁸

Many of the RCTs discussed recommendations for further studies on aprepitant. Diemunsch et al and Gan et al both recommended further studies be conducted to determine its effectiveness in prevention of PONV in other patient populations such as pediatrics.^{7,9} Diemunsch et al also recommended further studies on the use of aprepitant in (1) treatment of surgical patients who already have symptoms of nausea and vomiting (2) combination with a TIVA approach and (3) combination with other antiemetics as part of a multimodal regimen for PONV prophylaxis.⁷ Jeyabalan et al discussed the importance of determining the most optimal dose of aprepitant in prevention and treatment of postoperative nausea and vomiting.¹⁴ Jeyabalan et al

recommended further studies be conducted to determine aprepitant's potential interactions with other antiemetics as well as the cost effectiveness of its use.¹⁴

Risk of Bias

Based on the Cochrane Collaboration Risk of Bias tool, there are five sources of bias that may be evident within a study: selection, performance, detection, attrition, and reporting bias.¹⁹ Overall, this systematic review had a low risk for selection bias across the RCTs involved. Diemunsch et al, Diemunsch et al, Gan et al, and Jeyabalan et al utilized computerized randomization to select patients for inclusion which eliminated any selection bias.^{7,9,13,14} Ham et al and Lim et al did not mention how patients were selected for inclusion.^{15,16} Sinha et al and Vallejo et al recruited patients on the day of surgery.^{17,18} Sinha et al did not specify who recruited subjects; however, Vallejo et al mentioned that the anesthesiologists involved in care recruited patients to be subjects in the study.^{17,18} Therefore, Ham et al, Lim et al, Sinha et al, and Vallejo et al all had a high risk for selection bias based on the Cochrane Collaboration Risk of Bias tool.^{15,16,17,18,19} Allocation of patients was done by computer randomization in all 8 RCTS. Since allocation was concealed, this avoided selection bias. All RCTs were double-blinded, meaning that both the investigator and the patient were blinded to the study, except for Lim et al which did not specify if the investigator knew of the assigned group.^{7,9,13,14,15,16,17,18} Therefore, this systematic review has a low risk for performance and detection bias.¹⁹

DISCUSSION

Summary of Evidence

Eight RCTs were included in this review, which resulted in a total of 4,011 male and female patients age 18 years and older. Two systematic reviews that were also included in this review studied aprepitant with ondansetron as well as other antiemetics such as decadron. All ten studies included in the review were considered Level I evidence based on John's Hopkin's toolkit.¹² The majority of the articles were also considered high quality evidence, with the exception of 3 articles that were considered good quality.¹² Given the limited number of studies

on aprepitant versus ondansetron, the investigators were unable to maintain a selective patient population. Therefore, both males and females were included with a variety of different surgical procedures. Nausea severity, retching, vomiting, and use of rescue antiemetics were used as study points to measure the antiemetic efficacy of aprepitant in comparison to the most commonly used antiemetic, ondansetron. These measures were evaluated for 48 hours postoperatively in most of the studies, except for one study that measured nausea for 24 hours and another that measured nausea for 72 hours. A summary of the results of this systematic review are stated below:

- Preoperative administration of aprepitant provides superior protection against nausea, vomiting, and need for rescue antiemetics in comparison to ondansetron 4 mg IV.¹³
- Administration of aprepitant in combination with ondansetron is more effective than administration of ondansetron alone in prevention of PONV.^{15,16,17,18}
- Aprepitant is superior to ondansetron in prevention of postoperative vomiting.^{7,9,13}
- Preoperative administration of aprepitant delays time to first vomiting episode.^{7,15,16,17}
- Patients who receive aprepitant preoperatively are two times as likely to be protected against vomiting in comparison to those who receive ondansetron.⁷

Limitations to this Systematic Review

There are a number of apparent limitations to this systematic review that must be mentioned. Given the limited number of studies conducted comparing aprepitant to ondansetron, the investigator was unable to conduct a systematic review with studies that looked at one type of surgical procedure. Therefore, patients included in the review had variety of different procedures including open abdominal, laparoscopic gynecological, rhinolaryngeal, outpatient plastic, breast, thyroid, and bariatric surgeries. Given the large variety of different procedures, patients included in the study may have varying degrees of nausea in the postoperative period. Additionally, both males and females were included in this systematic review. As previously discussed, females have at least a 20% risk for developing PONV in comparison to males who have no increased risk

for PONV based on gender.⁶ Therefore, including both females and males could have affected nausea scores.

Different doses of aprepitant and ondansetron were administered throughout each of the studies. Aprepitant was given at doses of 40 mg, 80 mg, and 125 mg based on the study and ondansetron was given at a dose of 4 mg in most studies, except for 8 mg in one study. All doses of aprepitant were administered prior to induction of anesthesia; however, ondansetron was given at different time periods in the perioperative period which could have influenced the severity of nausea. Lastly, use of rescue antiemetics that were used by patients who had complaints of nausea in some studies could undoubtedly have influenced nausea scores in the postoperative period.

Recommendations for Future Systematic Reviews

Given the above discussed limitations, future systematic reviews should be conducted that focus on one specific patient population, preferably the female population given the increased risk for PONV. One specific procedure or area of surgery, such as laparoscopic gynecological or abdominal surgery, should be focused on to eliminate the differing effects of the surgical procedure on severity of nausea experienced postoperatively. Additionally, studies included in the review should be those with the same dose of aprepitant and ondansetron given at the same time in the perioperative period. Systematic reviews in the future should also utilize studies that measured the severity of nausea at the same time postoperatively, with the same scoring system.

Facilitators and Barriers

One facilitator to the use of aprepitant is its ease of administration. Aprepitant is a one-time administration by mouth, that does not require subsequent doses because of its long half-life of 40 hours.⁹ The majority of other antiemetics in use require redosing, like the commonly administered ondansetron. A major barrier to the use of aprepitant is the cost. For example, the institution involved in the study conducted by Vallejo et al reported a cost of \$0.60 for ondansetron in comparison to \$46.60 for aprepitant.¹⁸ Therefore, patients must be willing to pay additional costs to prevent postoperative nausea and vomiting.

Recommendations for Practice

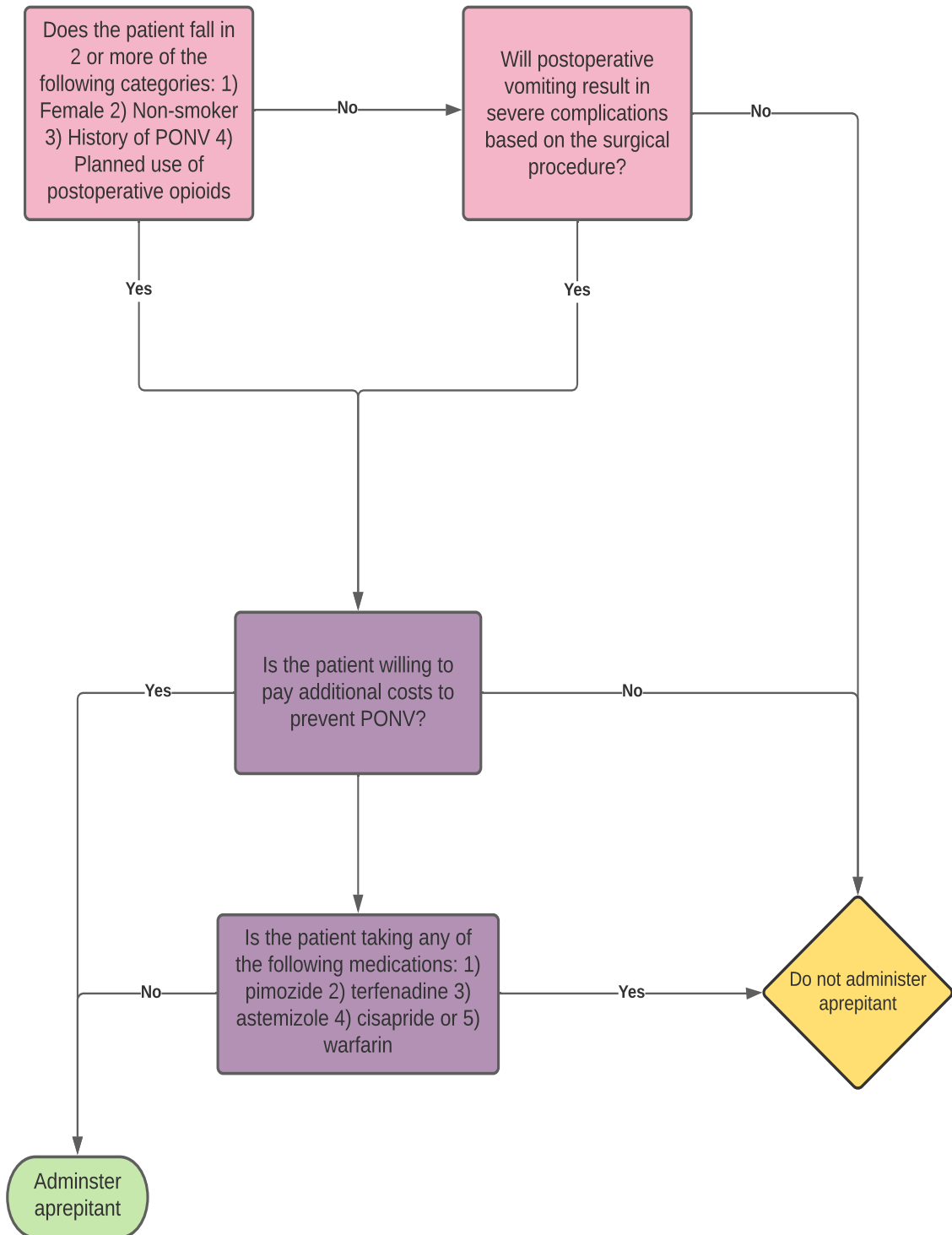
Based on the findings from this systematic review, it is clear that aprepitant has demonstrated improved efficacy over ondansetron in prevention of PONV. Aprepitant notably contributes to delayed time to first vomiting, which may be related to its long half-life. Therefore, it may be particularly useful in patients whom vomiting in the direct postoperative period may lead to serious complications. For example, Diemunsch et al suggested that aprepitant may be especially useful in surgeries requiring postoperative jaw-wiring.⁷ As previously discussed, use of antiemetics from different drug classes proves to be more efficacious than that of single agent antiemetic therapy.⁸ The ASA recommends use of 1 or 2 interventions for patients at moderate risk for PONV, and 2 or greater interventions for those at high risk for PONV.⁹ Therefore, use of aprepitant in combination with ondansetron may be beneficial in those at risk for PONV, such as patients of female gender, with a non-smoking history, with a history of PONV, or those with planned use of postoperative opioids.⁶ An algorithm for use of aprepitant is displayed in Figure 2.

Conclusion

The aim for this systematic review was to determine if the administration of aprepitant, including the combination of aprepitant with ondansetron, would be more effective than ondansetron alone in reducing the incidence rates of PONV in patients 18 years or older undergoing general anesthesia. Based on the evidence obtained from ten different research articles, aprepitant administered alone along with aprepitant administered with ondansetron is more effective than ondansetron alone in reducing PONV rates. While aprepitant may not be cost efficient in the patient at low risk for PONV, it has the potential to be extremely beneficial in patients at high risk for PONV. Administration of aprepitant preoperatively was particularly effective in prevention of postoperative vomiting and time to first vomiting episode.^{7,9,13,15,16,17} Therefore, aprepitant may also be valuable in cases in which postoperative vomiting could lead to serious adverse effects, such as the patient requiring postoperative jaw-wiring.⁷

It is clear that postoperative nausea and vomiting is an ongoing problem despite a multitude of improvements in healthcare. PONV rates remain high despite the availability of multiple antiemetic agents and short-acting anesthetic agents, as well as the development of minimally invasive surgical techniques.² Patients have indicated prevention of PONV as being one of the most concerning effects of receiving general anesthesia and have agreed to pay up to \$100 out of pocket to avoid experiencing nausea or vomiting postoperatively.² Implementation of an evidence-based algorithm for administration of aprepitant has the potential to lead to improved patient outcomes and increased patient satisfaction. An algorithm can help anesthesia providers identify high risk patients who would benefit from administration of aprepitant. This systematic review has demonstrated aprepitant's effectiveness in the prevention of postoperative nausea and vomiting, and a change to current practice is warranted.

Figure 2. Aprepitant administration algorithm



DNP PROJECT ACTION PLAN

Primary Aim

Postoperative nausea and vomiting (PONV) is one most common patient complaints reported after surgery.¹ In one study, surgical patients rated vomiting as the number 1 most concerning possible anesthesia outcome.¹ PONV contributes to patient dissatisfaction with anesthesia, lengthened post-anesthesia recovery unit stays, and increased healthcare costs.³ It can cause complications such as pulmonary aspiration, wound dehiscence, esophageal rupture, pneumothorax, subcutaneous emphysema, and unplanned hospital admission.³ Despite a multitude of improvements today in healthcare, including the availability of multiple prophylactic antiemetic agents, the use of minimally invasive surgical techniques, and the availability of short-acting anesthetics, PONV rates still remain high.² Incidence rates for inpatient surgeries range between 30% to 50%, with rates as high as 70% to 80% for patients with multiple risk factors.³ It is important to stay abreast with the most current evidence-based literature in order to combat the continued high rates of PONV.

Recent evidence suggests that the NK-1 antagonist, aprepitant, can be remarkably effective in the prevention of PONV. When aprepitant is administered in combination with ondansetron, it shows improved effectiveness compared to ondansetron alone. A significant advantage of aprepitant is its ability to reduce the incidence of postoperative vomiting. Aprepitant may hold high value in the patient at increased risk for PONV or increased risk for serious adverse effects in the presence of postoperative vomiting. Recommendations for use of aprepitant include its use in patients with an Apfel score of 2 or >, or at moderate to high risk for PONV, and in patients at risk for serious complications related to postoperative vomiting such as those that require post-operative jaw-wiring. Implementation of an educational module in the form of a PowerPoint presentation to educate anesthesia providers on aprepitant's use will be the doctorate in nursing practice (DNP) action plan and quality improvement (QI) project.

Goals and Outcomes

The overlying goal for this DNP is to educate anesthesia providers through a PowerPoint presentation in order for them to make informed decisions and incorporate the use of aprepitant in their practice. By doing this, the goal is to contribute to decreasing rates of PONV. In order to evaluate the goals for this DNP project, the SMART model framework was used.²⁰ This framework is based on the idea that goals should be SMART, which stands for specific, measurable, achievable, results focused and timely.²⁰ Utilizing this framework ensures that goals are clearly stated, well-defined, and easily measured. Listed in Figure 3 below are the SMART goals developed for this DNP project.

Figure 3. SMART Goals

Initial Goal: All anesthesia providers will be educated through a PowerPoint Presentation on the use of aprepitant for the prevention of PONV. A pre-test and post-test survey will be distributed electronically to determine the effectiveness of the educational module. Included in the Powerpoint presentation will be a background of the problem, evidence-based findings, and recommendations for practice.

- **Outcome # 1:** By the end of the summer, anesthesia providers will be able to discuss the significance of the problem of PONV and ways in which aprepitant can contribute to decreasing rates.

Intermediate Goal: Anesthesia providers will have an increased knowledge base on the NK-1 receptor antagonist, aprepitant, and be able to state the most appropriate use of aprepitant in the prevention of PONV.

- **Outcome #2:** Anesthesia providers will score at least 10 % higher on the post-test survey.
- **Outcome #3:** Anesthesia providers will be able to state two appropriate uses for aprepitant in the prevention of PONV such as a patient with an Apfel score of 2 or > or a patient who requires postoperative jaw wiring.

Long Term Goal: Anesthesia providers will state that they recognize the positive impact that aprepitant could have on decreasing PONV rates.

- **Outcome #4:** Anesthesia providers will state that they would utilize aprepitant in their practice and would recommend its use to their colleagues.

Ultimate Goal: Adopting aprepitant as part of the hospital's available medications for use and adding a protocol to the anesthesia group on the use of aprepitant.

IMPLEMENTATION

Setting and Participants

The quality improvement project was conducted via an online survey that included a PowerPoint educational module. This was distributed to the members of the Miami Beach Anesthesiology Associates group at Mount Sinai Medical Center. The participants in the preliminary study group included anesthesia providers with the title of Certified Registered Nurse Anesthetist (CRNA) and Anesthesiologist. Participants included in this study were based on an email list provided by Miami Beach Anesthesiology Associates as part of the anesthesia group that employs Mount Sinai Medical Center. Participants were asked to complete a pre-survey questionnaire as well as a post-survey questionnaire to determine the effectiveness of the educational module in educating anesthesia providers on the use of aprepitant. The anticipated sample size was between 5-15 participants. After recruitment of subjects was completed, a total of 7 participants agreed and participated in this study.

Recruitment

The target population for this improvement project were anesthesia providers including CRNAs and anesthesiologists of whom work in a setting in which care is provided to patients greater than 18 years of age undergoing general anesthesia. Recruitment of participants was performed via an online invitation through an email list of anesthesia providers providing direct anesthesia care services to surgical patients at Mount Sinai Medical Center. Proposed participants were informed that participation in the study was voluntary and that participants have the right to withdraw from the study at any time.

Description of Approach and Project Procedures

This project was conducted via email distribution of a virtual educational module through an online survey software called Qualtrics. The educational module was viewed via a recorded PowerPoint presentation that was displayed through a YouTube video. This educational module contained information on the use and effectiveness of the anti-emetic drug, aprepitant, in the

prevention of PONV in adult patients undergoing general anesthesia. The primary goal for this intervention was to increase anesthesia providers' knowledge of aprepitant to provide anesthesia providers with the information needed to integrate aprepitant into their practice based on the evidence obtained from this systematic review. Anesthesia providers' existing knowledge on aprepitant was measured via a pre-survey questionnaire prior to viewing the YouTube video. The pre-survey questionnaire contained a total of 12 questions on PONV and aprepitant. After the video was viewed, participants filled out a post-survey questionnaire to determine the effectiveness of this educational intervention. The post-survey questionnaire was identical to the pre-survey questionnaire, which included the same 12 questions. The goal with the pre and post surveys was to test the content of the module to determine if the information contained within it was effective in the education of anesthesia providers on the antiemetic drug, aprepitant.

The YouTube video was recorded with audio on PowerPoint and uploaded to YouTube to be viewed by participants. It contained a total of 14 slides including the introduction and reference slides, and was approximately 7 minutes in length. The video included information regarding the background on PONV, the importance of addressing PONV, and complications related to PONV. Additional information included current recommendations for practice on prevention of PONV and a risk assessment tool that is used to determine patients' risk for developing PONV after general anesthesia. Information on the mechanism of action and proper administration of aprepitant was contained within the video. This included appropriate route and timing of administration, as well as half-life. This was compared next to the most commonly used anti-emetic, ondansetron. The educational module included information on the study findings of aprepitant that were discovered from this systematic review, including aprepitant's effectiveness in the prevention of PONV in comparison to ondansetron and in combination with ondansetron. Recommendations for practice on the use of aprepitant were included and a summary of information was provided to conclude the content of the video. The educational module offered anesthesia providers with evidence-based information obtained from multiple different studies as

mentioned within this systematic review. It allowed anesthesia providers the opportunity to utilize the information provided to make informed decisions on treatment of patients in the prevention of PONV.

Protection of Human Subjects

All participants that completed the educational intervention remained anonymous and data was secured utilizing unique code identifiers. Data collected for this project was protected with a laptop password and spyware. Only the project team was entitled access to the data obtained from this project. There were minimal risks associated with this project, as would be expected with any educational intervention. This could have included mild emotional stress or mild physical discomfort from sitting on a chair for approximately 20 minutes.

Data Collection and Analysis

The primary instruments used in this study to collect data include the pre-survey questionnaire and the post- survey questionnaire which were compared to one another to determine the effectiveness of the educational module on anesthesia providers knowledge of aprepitant in the prevention of PONV. As previously mentioned, the Qualtrics survey software program was utilized to distribute and collect data. Unique code identifiers were utilized for participants that kept participants anonymous to link the pre and post survey questionnaires to the same participant, in order to more accurately determine the effectiveness of the educational intervention. The pre-survey questionnaire was intended to determine participants baseline knowledge of aprepitant, while the post-survey questionnaire was intended to determine the ability of the educational module to effectively deliver appropriate information on aprepitant. The data collected in this study remained secured throughout the process, with no participant identifiers recorded during any part of the study.

Data Management and Measure

The investigator for this project was the DNP student of whom was responsible for disbursement of surveys to the email list provided by Miami Beach Associates anesthesia group.

The DNP student was also responsible for collection and measurement of data within the Qualtrics software system. Each question was measured, and the responses were evaluated to identify Mount Sinai Medical Center anesthesia providers' knowledge base on aprepitant. No personal identifiers were recorded that could be viewed by the investigator. However, a unique code was utilized to link the same participant to the pre and post survey respectively to accurately measure responses. The value of this educational module was based upon the results of the pre and post survey instruments. Through statistical analysis, the results will determine if the educational module increased anesthesia providers' knowledge on aprepitant.

IMPLEMENTATION RESULTS

Pre/Post-Test Demographics

The pre-test demographics are as displayed in Table 4., shown below.

Table 4. Pre-Test Participants Demographics

Demographic	n (%)
Total Participants	7 (100%)
<i>Gender</i>	
Male	3 (43%)
Female	4 (57%)
<i>Age</i>	
18-29	1 (14%)
30-49	6 (86%)
40-60	0 (0%)
> 60	0 (0%)
<i>Ethnicity</i>	
White	5 (72%)
Asian	0 (0%)
Black or African American	1 (14%)
Native Hawaiian or Pacific Islander	0 (0%)
Other	1 (14%)
<i>Years of Experience</i>	
1 to 2 years	2 (28.5%)
3 to 5 years	2 (28.5%)
6 to 10 years	0 (0%)
More than 10 years	3 (43%)

There were 7 participants in total that participated in this improvement project. Between the 7 participants, 4 were females (57%) and 3 were males (43%). The majority of participants were between the ages of 30 and 49 years old (n= 6, 86%). The only other age group that participated in this study was between 18 and 29 years old (n=1, 14%). The ethnicities represented within this participant group include white (n=5, 72%), black or African American (n= 1, 14%), and other (n=1, 14%). The participants were asked the number of years of experience they have been practicing anesthesia. There was a range in number of years of experience within the study group including: 1 to 2 years (n= 2, 28.5%), 3 to 5 years (n=2, 28.5%), and more than 10 years (n=3, 43%).

Pre-Test Results on Likelihood to Use and Recommend Aprepitant

The pre-survey questionnaire asked participants their perception on the effectiveness of aprepitant in PONV prevention, how likely they were to use aprepitant in their practice, and how likely they were to recommend aprepitant to other anesthesia providers. The goal was to determine if this educational module would change anesthesia providers' perceptions of aprepitant, their willingness to incorporate it into their practice, and their likelihood to recommend it to other anesthesia providers. Most participants perception of aprepitant in the pre-test survey was that aprepitant's antiemetic effects are effective (n=5, 72%). The last two participants response to the pre-test survey were that aprepitant's antiemetic effects are somewhat effective (n=1, 14%) and most ineffective (n=1, 14%). When asked how likely participants were to use aprepitant in the prevention of PONV on the pre-test, participants responses were as follows: most likely (n=1, 14%), somewhat likely (n=5, 72%), and somewhat unlikely (n=1, 14%). Participants were either most likely (n=3, 43%) or somewhat likely (n=4, 57%) to recommend aprepitant to other anesthesia providers.

Pre-Test and Post-Test Results on Knowledge of PONV and Aprepitant

The survey focuses on determining anesthesia providers current perceptions on PONV, effectiveness of current practices, and the implications for not addressing the current issue of

PONV. It also addresses the mechanism of action, pharmacological properties, and effectiveness of aprepitant in the prevention of PONV. The majority of study participants were not able to answer correctly to the rates of PONV for inpatient surgeries and to rates of PONV in patients with multiple risk factors in the pre-test survey. Only 1 participant answered correctly to both of these questions. All participants answered these questions correctly in the post-test survey. Only 3 out of 7 participants were aware that vomiting has been reported as one of the most concerning possible anesthesia outcomes in the pre-test survey, and all participants answered correctly in the post-test survey. In the pre-test survey, 57% (n=4) answered correctly to aprepitant’s mechanism of action, whereas in the post-test survey all respondents answered correctly. The majority of participants did not understand the pharmacological properties of aprepitant in the pre-test survey with only 2 (29%) participants answering correctly. All respondents answered the question on the pharmacological properties of aprepitant correctly on the post-test survey. Complications of PONV and consequences of failing to address PONV as a problem was well understood by all participants in the pre-test survey. The differences between Pre- and Post-test responses are displayed in Table 5.

Table 5. Differences in Pre- and Post-Test Knowledge

Questions	Pre-test	Post-test	Difference
Postoperative nausea and vomiting (PONV) rates for inpatient surgeries range between:	14%	100%	86%
Patients with multiple risk factors experience postoperative nausea and vomiting (PONV) at rates as high as:	14%	100%	86%
Complications of PONV include:	100%	100%	0%
Patients have reported that _____ is one of the most concerning possible anesthesia outcomes.	43%	100%	57%
Failure to address PONV as a problem will result in:	100%	100%	0%
All of the following are independent risk factors for PONV according to the Apfel scoring system, EXCEPT:	86%	100%	14%

Patients given antiemetics such as the commonly used 5-HT3 antagonist, ondansetron, still experience PONV _____ of the time.	0%	14%	14%
Aprepitant exerts its antiemetic effects via:	57%	100%	43%
All of the following are true of aprepitant EXCEPT:	29%	100%	71%

Post-Test Results on Likelihood to Use and Recommend Aprepitant

In the post-test questionnaire, 6 participants (86%) responded that aprepitant's antiemetic effects are effective, and 1 participant (14%) responded that aprepitant's antiemetic effects are somewhat effective. Overall, respondents reported that they were more likely to use aprepitant in the prevention of PONV after viewing the YouTube video. In the pre-test survey 1 participant responded they were most likely to use it, 5 participants responded they were somewhat likely to use it, and 1 participant responded they were somewhat unlikely to use it. However, in the post-test survey, 4 participants responded that they were most likely to use aprepitant in the prevention of PONV and 3 responded that they were somewhat likely to use it. Lastly, in the pre-test survey 3 participants reported that they were most likely to recommend the use of aprepitant to other anesthesia providers and 4 participants reported they were somewhat likely to recommend its use. In the post-test survey, more participants (n= 5, 71%) were most likely to recommended aprepitant to other anesthesia providers in comparison to the pre-test survey (n=3, 43%). The rest of the participants (n=2, 29%) in the post-test survey reported they were somewhat likely to recommended aprepitant to other anesthesia providers.

Summary

Overall, the results from the pre and posttest surveys reflected an improvement in participant knowledge on PONV and the antiemetic drug, aprepitant. In the pre-test survey, the mean score was 49%, whereas in the post-test survey the mean score was 90%. This showed an increase of 41% on anesthesia provider knowledge. Additionally, more participants reported that

they were most likely to use aprepitant in the prevention of PONV and recommend aprepitant to other anesthesia providers in comparison to the pre-test responses.

IMPLEMENTATION DISCUSSION

Limitations

Limitations to this study include the small sample size of only 7 participants. The email list provided by Miami Beach Anesthesiology Associates anesthesia group contained 31 people. However, only 7 responded and agreed to participate in this study. A larger sample size would have been preferred to obtain the most accurate results that would more appropriately reflect Mount Sinai Medical Center's anesthesia providers. Another limitation is that the survey link was sent out and only available for approximately 1 month. A longer time frame could have results in a larger sample size, and a more representative sample population. Lastly, the project was conducted exclusively online, which prevented it from being dispersed by other means that may have yielded a larger sample size as well.

Future Implications for Anesthesia Practice

The practice of anesthesia requires providers, including CRNAs and anesthesiologists, to stay abreast regarding the most current evidence for treatment of patients in the perioperative period. This includes remaining up to date on newer pharmacological therapies such as aprepitant in the prevention of PONV. Educational modules, such as the one utilized in this study, can be helpful and effective in educating anesthesia providers on such updates within anesthesia. Short and concise presentations such as the 7-minute recorded PowerPoint presentation on PONV and aprepitant can add value to the anesthesia practice and allow providers to make more informed decisions on use of new therapies.

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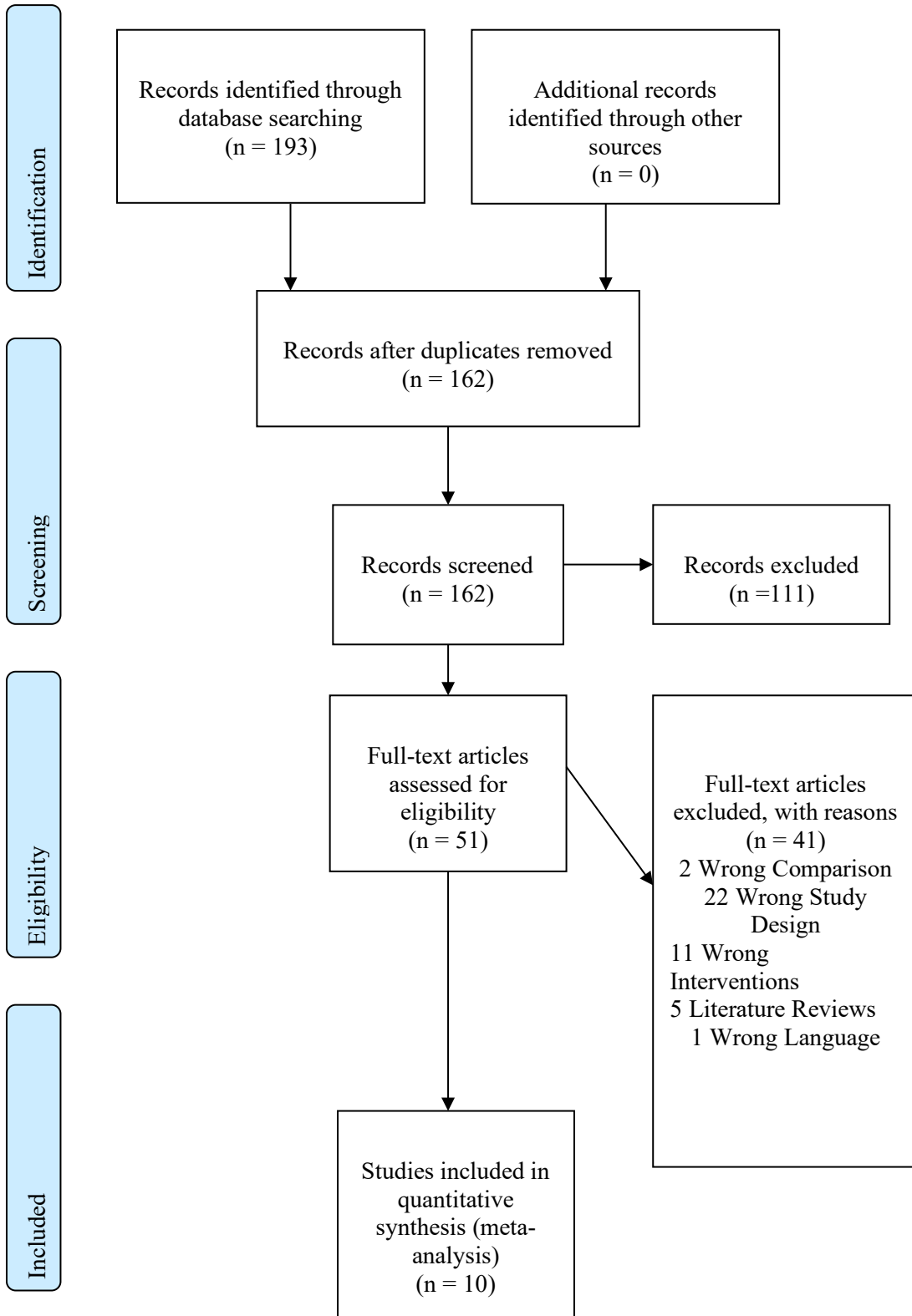
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Appendix

Appendix A: PRISMA Flow Diagram



Appendix B: Matrix Table

<p>Diemunsch P, Apfel C, Gan TJ, et al., 2007,</p> <p><i>Preventing postoperative nausea and vomiting: post hoc analysis of pooled data from two randomized active-controlled trials of aprepitant</i></p>	<p>Post hoc analysis of pooled data from two randomized active-controlled trials of aprepitant.</p> <p>Patients undergoing general anesthesia were randomly assigned to 3 different groups to receive a preoperative dose of: (1) aprepitant 40 mg PO (2) aprepitant 125 mg PO or (3) ondansetron 4 g IV, in two randomized, double-blind clinical trials.</p>	<p>Sample size: 1599 patients Population: patients 18 years or older, ASA I-III, open abdominal surgery requiring overnight stay. 92% female population, Mean age= 46, 82% Gynecological surgery, 18% Non-gynecological surgery</p> <p>Exclusion criteria: breast feeding patients, patients requiring orogastric (OG)/nasogastric (NG) tube, patients receiving neuraxial or propofol based anesthesia</p>	<p>IV1: Aprepitant 40 mg PO IV2: Aprepitant 125 mg PO IV3: Ondansetron 4mg IV DV1: nausea DV2: episodes of vomiting DV3: use of rescue therapy</p> <p>Aprepitant or placebo was given 1–3 hours before anticipated induction of anesthesia, and intravenous ondansetron or placebo was infused over 2–5 minutes immediately prior to induction.</p>	<p>Nausea was rated on a verbal rating scale (VRS) on a scale of 0-10 where 0=no nausea and 10=nausea as bad as it could be.</p> <p>Data was analyzed using SAS version 8.2. A value of > 1.0 for the odds ratio favored aprepitant to ondansetron.</p> <p>Any episodes of vomiting and use of rescue therapy were recorded by a study coordinator for the first 48 h postop. In addition, nausea assessments were administered by a study coordinator at 2, 4, 6, 24 and 48 hours after surgery, at any time the patient complained of nausea, and just prior to administration of rescue therapy.</p>	<p>No significant nausea: -Aprepitant 40mg: 56.4% -Aprepitant 125 mg: 55.1% -Ondansetron 4mg: 48.1% No nausea: -Aprepitant 40mg: 39.6% -Aprepitant 125 mg: 36.5% -Ondansetron 4mg: 33.1% No vomiting: Aprepitant 40mg: 86.7% -Aprepitant 125 mg: 90.2% -Ondansetron 4mg:72.4% No nausea or vomiting: Aprepitant 40mg: 38.3% -Aprepitant 125 mg: 35.9% -Ondansetron 4mg: 31.4% No nausea, vomiting, or rescue: Aprepitant 40mg: 37.9% -Aprepitant 125 mg: 35.3% -Ondansetron 4mg: 31.2%</p>	<p>-Both doses of aprepitant showed greater protection over ondansetron against nausea that occurred with or without vomiting, or in combination with vomiting and a need for rescue medication. -In general, more patients who had received aprepitant reported lower scores of nausea than those who received ondansetron.</p>	<p>Aprepitant may be more effective than ondansetron in prevention of vomiting, and aprepitant at a dose of 40 mg may be more effective than ondansetron in prevention of nausea. Aprepitant 125 mg tended to show more similarity or slighted reduced effect compared with 40 mg of aprepitant.</p>	<p>Level I evidence</p> <p>Good quality evidence</p> <p>Strengths: consistency of findings, large sample size</p> <p>Limitations: -post hoc nature of the data -use of rescue therapy and its potential influence on nausea and/or vomiting</p>
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<p>Diemunsch P, Gan TG, Philip BK, et al., 2007.</p> <p><i>Single-dose aprepitant vs ondansetron for the prevention of postoperative nausea and vomiting: a randomized, double-blind Phase III trial in patients undergoing open abdominal surgery</i></p>	<p>Randomized double-blind controlled trial</p> <p>Patients receiving general anesthesia for major abdominal surgery were randomly assigned to 3 different groups to receive a preoperative dose of: (1) aprepitant 40 mg PO (2) aprepitant 125 mg PO or (3) ondansetron 4 g IV within 3 hours of induction of anesthesia</p>	<p>Sample size: 992 Population: Age 18 years or older, ASA I-III Surgical procedure: Open abdominal surgery</p> <p>Exclusion criteria: breast feeding patients, patients requiring orogastric (OG)/nasogastric (NG) tube, patients receiving neuraxial or propofol based anesthesia</p> <p>Setting: 42 centres (8 U.S. sites and 34 non-U.S. sites in North America, South America, Europe, Australia, and Asia)</p>	<p>IV1: Aprepitant 40 mg PO IV2: Aprepitant 125 mg PO IV3: Ondansetron 4mg IV DV1: nausea</p>	<p>Verbal rating score (VRS) was used to rate nausea from 0, or no nausea, to 10, or nausea as bad as it can be. This was measured at 2,6,24, and 48 hours after surgery, at any time the patient complained of nausea, and just before receiving rescue antiemetics.</p> <p>-Poisson regression analysis was done to rate the incidence of vomiting and compare between the groups.</p>	<p>For the no vomiting endpoint, the study had 99% power to detect a 15 percentage-point difference between aprepitant 125 mg and ondansetron.</p>	<p>-Patients taking aprepitant 2x as likely to be protected from vomiting compared to patients taking ondansetron, & aprepitant delayed the time to first vomiting in comparison with ondansetron. -There was no statistically significant difference in the efficacy of 40 vs 125 mg PO of aprepitant. Aprepitant at 40 mg appeared to be adequate to prevent nausea/vomiting.</p>	<p>-Aprepitant is superior to ondansetron in protection against vomiting and nausea. -Aprepitant may be extremely beneficial in patients in which postoperative vomiting could lead to serious complications, such surgeries requiring jaw-wiring.</p>	<p>Level I evidence</p> <p>High quality evidence</p> <p>Strengths: findings consistent with literature, large sample size, Multicenter</p> <p>Limitations: -The timing of administration of ondansetron may have had an effect its efficacy. -Use of rescue therapy may have had an impact on incidences of nausea and vomiting.</p>
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<p>Gan TJ, Apfel CC, Kovac A, et al., 2007.</p> <p><i>A Randomized, Double-Blind Comparison of the NK1 Antagonist, Aprepitant, Versus Ondansetron for the Prevention of Postoperative Nausea and Vomiting</i></p>	<p>Randomized, Double-blind trial</p> <p>-Patients undergoing general anesthesia with nitrous oxide and volatile anesthetics for abdominal surgery were placed in 1 of 3 different groups to receive a preoperative dose of: (1) aprepitant 40 mg PO (2) aprepitant 125 mg PO or (3) ondansetron 4 g IV within 3 hours of induction of anesthesia</p>	<p>Sample size: 805</p> <p>Population: Age 18 years or older, ASA I-III</p> <p>Exclusion criteria: breast feeding patients, patients requiring orogastric (OG)/nasogastric (NG) tube, patients receiving neuraxial or propofol based anesthesia. Patients who vomiting with the last 24 hours before surgery</p> <p>Setting: 29 centers</p>	<p>IV1: Aprepitant 40 mg PO</p> <p>IV2: Aprepitant 125 mg PO</p> <p>IV3: Ondansetron 4mg IV</p> <p>DV1: nausea</p> <p>Patients were allocated to a treatment group within each clinical site using a computer-generated random allocation schedule stratified according to gender.</p> <p>-Patients received aprepitant or placebo 1-3 h before anticipated induction of anesthesia, and ondansetron or placebo by push over 2-5 min before induction.</p>	<p>Verbal rating score (VRS) was used to rate nausea from 0, or no nausea, to 10, or nausea as bad as it can be. This was measured at 2,6,24, and 48 hours after surgery, at any time the patient complained of nausea, and just before receiving rescue antiemetics.</p> <p>Emetic episode was defined as one or more continuous episodes of vomiting (oral expulsion of stomach contents) or retching (an attempt to vomit that is not productive of stomach contents); distinct episodes were those occurring at least 1 min apart.</p>	<p>Poisson regression analysis was used to compare rates of incidence of vomiting between treatment groups, which included factors for use of rescue antiemetics.</p>	<p>There was a 90% power to detect a 15 %-point difference between the aprepitant 125 mg group and the ondansetron group for the primary end point. This was based on a 50% response rate for ondansetron and 65% for aprepitant 125 mg.</p>	<p>The primary hypothesis—that aprepitant would be superior to ondansetron for complete response 0-24 h after surgery—was not met.</p> <p>- However, prevention of vomiting was superior in the aprepitant group for both the 24 and 48h postoperative periods.</p>	<p>Level I quality</p> <p>High quality</p> <p>Strengths: Good sample size, additional analysis accounted for rescue therapy found that for every 1 episode of vomiting in the aprepitant group, there were 4-7 episodes in the ondansetron group</p> <p>Limitations: use of rescue therapy, timing of ondansetron administration, subjectiveness of nausea</p> <p>Recommendations for further research: to demonstrate efficacy of aprepitant in other populations including the pediatric population</p>
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<p>Ham SY, Shim YH, Son MJ, et al., 2016.</p> <p><i>Aprepitant for antiemesis after laparoscopic gynaecological surgery</i></p>	<p>Randomised controlled trial</p> <p>-Patients undergoing laparoscopic gynaecological surgery that were planned to be on a fentanyl based patient-controlled analgesia (PCA) after postoperatively were given either oral aprepitant or placebo 1 h before anesthesia in combination with ondansetron 4 mg IV at the end of surgery along with 12 mg added to the PCA solution.</p>	<p>Sample size: 125 female patients, ages 22-55 years, ASA 1 & II, median Apfel= 3</p> <p>Procedure: gynecological laparoscopy with planned post-operative fentanyl based intravenous PCA</p> <p>Exclusion criteria: patients with allergies to aprepitant; patients taking drugs that interact with aprepitant including: pimozide, terfenadine, astemizole, cisapride and warfarin; patients taking other antiemetics before surgery; hepatic dysfunction or significant psychiatric disease or mental retardation</p> <p>Setting: Single-centre, major university hospital in Seoul, Korea</p>	<p>IV1: Aprepitant 80 mg PO 1 h before anesthesia</p> <p>IV2: Placebo 1 h before anesthesia</p> <p>DV: Ondansetron 4 mg</p> <p>-a sealed envelope was given only to the nurse who was not part of the study in order to prepare the assigned drug. Anesthesiologists in charge of patients were blinded to the assigned groups</p>	<p>Verbal Numerical Rating Score (VNRS) was used to measure the intensity of nausea (0= no nausea, 10= worst nausea imaginable). A nurse blinded to the study was assessed VNRS scores at 4 different points: (1) 10 min after admission to the PACU (2) PACU discharge to 6 hrs (3) 6-24 hrs (4) 24-48 hrs after surgery</p>	<p>Comparisons between the two groups were made using χ^2 test, fisher's exact test or Student's t-test. No significant differences in the two groups in terms of patient characteristics and operative procedures.</p>	<p>No significant difference in overall complete response in the first 48 h after surgery. However, the complete responses in the aprepitant and ondansetron group was higher in the PACU and up to 24 h after surgery. No difference in incidence of retching or vomiting, severity of nausea, or use of rescue antiemetics. Incidence of nausea was lower in the aprepitant/ondansetron group in PACU and 24 h after surgery. Time to first PONV was delayed in the aprepitant/ondansetron group as well.</p>	<p>Aprepitant in combination with ondansetron delayed the time to first PONV and reduced the incidence of nausea in the PACU.</p> <p>Aprepitant administration should be considered based on cost as well and patient willingness to pay.</p> <p>The study concluded that aprepitant 80 mg with ondansetron was superior to ondansetron alone in preventing early PONV.</p>	<p>Level I Evidence</p> <p>High quality</p> <p>Limitations: (1) the sample sizes was selected based on incidence of PONV, which was different from the original endpoint of complete response to PONV and use of rescue antiemetics (2) the data was collected at any point towards the end of the assessment period (3) the dose of 80 mg was higher than the FDA approved dose for PONV</p>
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<p>Jeyabalan S, Thampi SM, Karuppusami R, Samuel K., 2019.</p> <p><i>Comparing the efficacy of aprepitant and ondansetron for the prevention of postoperative nausea and vomiting (PONV): A double blinded, randomised control trial in patients undergoing breast and thyroid surgeries.</i></p>	<p>Double blinded, randomised control trial</p> <p>Patients undergoing breast and thyroid surgeries were randomly assigned to 2 groups: (1) 1 cap of placebo preoperatively and ondansetron 4mg IV at the end of surgery and every 8 hours thereafter up to a total of 3 doses and (2) PO Aprepitant pre-operatively and placebo injection at the end of surgery and every 8 hours thereafter up to 3 doses.</p>	<p>Sample size: 125</p> <p>Population: Females, Age 18 -65 years, ASA I-II</p> <p>Exclusion criteria: any patient on antiemetic or steroid therapy, or any drug known to cause emesis, pregnant or nursing mothers, patients with known allergy to ondansetron or aprepitant</p> <p>Setting: tertiary care hospital</p>	<p>IV1: Ondansetron IV2: Aprepitant</p> <p>DV1: vomiting DV2: # of emetic episodes DV3: severity of postoperative nausea DV4: time to first vomiting episode DV5: use of rescue antiemetics DV6: patient satisfaction rating</p>	<p>Verbal rating scale (VRS): patients graded nausea from 0 ("no nausea") to 10 ("nausea as bad as it could be") at 0-2, 2-12 and 12-24 h after the operation.</p> <p>VRS 1-3: mild VRS 4-7: moderate VRS > 8: severe</p> <p>Nausea- an uncomfortable feeling that leads to a tendency to vomit. Retching -an effort to vomit which is not under voluntary control and that does not cause expulsion of stomach contents. Vomiting-an expulsion of stomach contents. Emetic episode- a single retch or vomit or any number of continuous vomits or retches.</p>	<p>Chi-square test, Fisher's exact test, & Yate's continuity correction were used to find the association between categorical variables and two groups.</p> <p>The nonparametric Mann-Whitney test was also used to compare the groups based on duration of anesthesia and time to first vomiting episode.</p> <p>All tests were two sided at $\alpha = 0.05$ level of significance.</p>	<p>2 h after surgery, the VRS for nausea in the: ondansetron group was 79.7% (n = 47) & in the aprepitant group was 83.6% (n = 51)</p> <p>2-12 h in the postoperative period: 81.4% of the ondansetron group and 75.4% in aprepitant group did not experience nausea</p> <p>ondansetron and aprepitant were equally efficacious in preventing emetic episodes, reducing the incidence of nausea and delaying the time to request of a rescue antiemetic.</p>	<p>A single dose of oral aprepitant has comparable effects to IV ondansetron in preventing PONV, the severity of nausea, number of rescue antiemetics, and the time to first emetic episode in the 24 h postoperative period.</p> <p>-Level I evidence -High quality evidence</p> <p>Strengths: comprehensive literature review, level of transparency Limitations: - Aprepitant 40 mg was used. Previous literature has shown improved efficacy with higher doses (80mg & 125 mg) of aprepitant. -Inconsistent findings with previous studies that found aprepitant to be more effective than ondansetron in prevention of vomiting at 24 and 48hrs after surgery</p>
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<p>Lim CS, Ko YH, Park SI, et al., 2013.</p> <p><i>Efficacy of the oral neurokinin-1 receptor antagonist aprepitant administered with ondansetron for the prevention of postoperative nausea and vomiting</i></p>	<p>Randomized controlled trial</p>	<p>Sample size: 90 patients</p> <p>Population: Age 18-65 years, ASA I-II</p> <p>Exclusion criteria: Pregnancy, patients who were administered perioperative anti-emetics, steroids, antihistamines, or psychiatric drugs.</p> <p>Procedure: Rhinolaryngological surgery</p>	<p>IV: Aprepitant 80 mg IV2: Aprepitant 125 mg DV: ondansetron 4 mg just before the end of surgery</p>	<p>Rhodes index of nausea, vomiting, and retching (RINVR) was examined at 6 h and 24 h after surgery.</p>	<p>Chi square test was utilized for comparison of the rate of PONV occurrence and of the patients who received rescue antiemetics. Bonferroni test was used for differences in demographic data of the patients.</p> <p>No statistical difference was found between the groups.</p>	<p>Rates of PONV occurrence measured at 6h was 29.2% (7/24) in the control group, 17.9% (5/28) in the Ap80 group, and 3.9% (1/26) in the Ap125 group. There was a significant statistical difference between the control group and Ap125 group(P=0.015).</p>	<p>The rates of PONV were lower in patients who received ondansetron 4 mg + aprepitant 125 mg in comparison to those who received only ondansetron 4mg.</p> <p>Level I Good quality</p> <p>Limitations: patients included in this study did not have a high degree of risk for PONV</p>
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<p>Liu M, Zhang H, Du B, et al., 2015.</p> <p><i>Neurokinin-1 Receptor Antagonists in Preventing Postoperative Nausea and Vomiting</i></p>	<p>Systematic Review and Meta-analysis</p> <p>Data was extracted from studies that measured the antiemetic effects of NK-1R antagonists in comparison to other drugs or a placebo</p> <p>Studies had to meet following criteria: RCTs assessing interventions to prevent PONV, trials comparing the antiemetic effects of NK-1R antagonists with that of other drugs or a placebo.</p>	<p>Population: 18 years or older, ASA I to III</p> <p>Setting: 5 multicenter studies, 9 single-centered studies</p> <p>Sample size: varies by study</p>	<p>IV: NK-1 antagonist (aprepitant, fosaprepitant, casopitant, ezlopitant, netupitant, CP122721, or vestipitant) for PONV prophylaxis</p> <p>DV1: incidence of nausea and vomiting</p> <p>DV2: rate of complete response defined as the absence of vomiting and no need of any rescue antiemetics</p> <p>DV3: incidence of use of rescue antiemetics and</p> <p>DV4: incidence of adverse events</p> <p>Control: placebo or ondansetron</p>	<p>RevMan Version 5.2 software (Cochrane Collaboration) was used for data syntheses</p> <p>A fixed-effects parametric approach was performed when no significant heterogeneity was found.</p>	<p>Incidence of vomiting: 3 studies with 1171 patients compared 40 mg aprepitant vs 4 mg ondansetron found aprepitant to be more effective in preventing vomiting. Aprepitant incidence was 13.3% and ondansetron incidence was 28.4%.</p> <p>Use of rescue drugs: no difference found between aprepitant and ondansetron</p> <p>Complete response: no significant difference between ondansetron and aprepitant</p> <p>Time to first vomiting: Meta-analysis of 3 studies using the fixed effects model showed that 40mg aprepitant could delay the time to first vomiting in comparison to ondansetron</p>	<p>Alonso-Damian et al. taking aprepitant had less nausea on arrival in the recovery room (3.3% vs 53.3%) and 6 hours after surgery (none vs 33.3%) compared with patients taking ondansetron.</p> <p>Meta-analysis of 2 studies with 1058 patients found that 125 mg of aprepitant was more effective in reducing the incidence of vomiting compared with 4 mg of ondansetron. Aprepitant incidence was 8.7% and ondansetron incidence was 27.5%.</p>	<p>All dosages of aprepitant (40, 80, and 125mg) were effective in reducing the incidence of postoperative vomiting but not the rates of nausea.</p> <p>When combined with a 5-HT3 receptor antagonist and dexamethasone, aprepitant could be more effective at reducing nausea but not vomiting. Therefore, NK1 antagonists may be more effective as combination therapy in the prevention of PONV.</p>	<p>-Level 1 evidence</p> <p>-High quality evidence</p> <p>Strengths: comprehensive literature review, transparency about limitations</p> <p>Limitations: different types of surgeries included could contribute to heterogeneity, patients had various levels of risk for PONV, some small-sampled, single centered studies included</p> <p>-More large high-quality trials are needed to determine the dose-related effect of aprepitant.</p> <p>-More studies need to focus on adverse events associated with NK-1 antagonists.</p>
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<p>Singh PM, Borle A, Rewari V, et al., 2016</p> <p><i>Aprepitant for postoperative nausea and vomiting: A systematic review and meta-analysis</i></p>	<p>Systematic Review and Meta-analysis</p> <p>Data was extracted from RCTs to compare the use of aprepitant to conventional antiemetics such as ondansetron and dexamethasone</p>	<p>Population: Adults >18 years undergoing elective surgery</p> <p>Setting: single and multicenter</p> <p>Sample size: varies based on study</p>	<p>IV: Aprepitant for PONV prophylaxis</p> <p>DV1: incidence of vomiting on POD1</p> <p>DV2: incidence of vomiting on POD2</p> <p>DV3: incidence of complete response on POD1</p> <p>DV4: incidence of complete response on POD2</p> <p>DV5: use of rescue therapy on POD1</p> <p>D6: use of rescue therapy on POD2</p>	<p>The I² statistic was used to quantify heterogeneity between the trials.</p> <p>Values of I² <40%: non-significant</p> <p>Values of 40-60%: moderate heterogeneity</p> <p>Values of 60-90%: high heterogeneity.</p> <p>-Results were expressed as Mantel-Haenszel pooled OR with 95% CI.</p> <p>-P<0.05 was considered statistically significant.</p> <p>The analysis of the data was performed using Comprehensive Meta-analysis V.2</p>	<p>Incidence of vomiting POD1: The OR for vomiting in the aprepitant group was 0.44 (95% CI 0.32 to 0.61) compared with other active controls (drugs). Vomiting incidence POD2: Vomiting occurred 6.8% of aprepitant patients compared with 12.8% of patients in the control groups. Incidence of complete response POD1: Aprepitant 29.1% compared with control group of 41.3%. Incidence of complete response POD2: Aprepitant 48.6% & control group 38.8%. Need for rescue antiemetics POD1: 35.6% of patients in aprepitant & 40.8% of patients in control. Need for rescue antiemetics POD2: 28.6% of patients in aprepitant group and 33.3% of patients in control group.</p>	<p>Aprepitant shows a clear improved efficacy, whether alone or combination with other antiemetics in the prevention of PONV.</p> <p>The incidence of vomiting on POD1 was significantly less in the aprepitant groups.</p>	<p>Aprepitant can lower the incidence of vomiting on POD1 and extend its therapeutic benefits into POD2. Compared with other antiemetics, aprepitant had a decreased need for rescue antiemetics and a greater number of patients had zero complaints of nausea/vomiting for a longer period of time.</p>	<p>Level I evidence</p> <p>High quality</p> <p>Strengths: Transparency of limitations, comprehensive search strategy and screening process</p> <p>Limitations: A wide range of doses of aprepitant were used. A wide range of surgeries were included. The heterogeneity between trials comparing aprepitant to conventional antiemetics remains relatively high. Therefore, higher quality evidence is needed for future research.</p>
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<p>Sinha AC, Singh PM, Williams NW, et al., 2014.</p> <p><i>Aprepitant's Prophylactic Efficacy in Decreasing Postoperative Nausea and Vomiting in Morbidly Obese Patients Undergoing Bariatric Surgery</i></p>	<p>Double-blind placebo-controlled trial</p>	<p>Sample size: 125 morbidly obese patients</p> <p>Population: ASA I to III patients aged 18 years or older, patient at high risk for PONV based on having 2 of the following: female, nonsmoker, history of PONV or motion sickness, planned use of opioids</p> <p>Exclusion criteria: allergy to ondansetron or aprepitant, pregnant or breastfeeding, patients with substance abuse or psychiatric disease, history of chronic nausea, pts taking medications with known antiemetic properties or those that interact with the medications being administered</p> <p>Setting: Hospital at the University of Pennsylvania in Philadelphia</p>	<p>IV1: Aprepitant 80 mg</p> <p>IV2: Placebo</p> <p>DV: Ondansetron 4 mg intraop</p> <p>In the postoperative period, a blinded observer (unaware to patient classification into groups A or P) recorded VRS nausea score for all the patients at 30 min, 1, 2, 6, 24, 48, and 72 h after the surgery.</p>	<p>Verbal rating score (VRS) from 0 to 10, where 0 was defined as "no nausea" and 10 was defined as "worst possible urge to vomit".</p> <p>Vomiting was defined as oral expulsion of gastric contents.</p> <p>Retching episode was defined as expulsive attempts without any oral content.</p> <p>Emetic episode was labeled as 3</p> <p>Complete response were those who had absolutely no nausea or vomiting without requiring rescue antiemetics.</p>	<p>Incidence of vomiting at 72 h was 3.1% (2/64) in the aprepitant group and 15% (9/60) in the placebo group (p=0.021, 95% confidence interval of difference)</p> <p>The odds ratio for a patient vomiting in the placebo group compared to aprepitant group was 5.47 times</p>	<p>The combination of aprepitant and ondansetron proved significantly better than ondansetron alone for preventing vomiting in morbidly obese patients undergoing laparoscopic bariatric surgery.</p> <p>Time to first vomiting was significantly prolonged in the aprepitant group, and the two vomiting episodes were seen only 6 h after the drug dose.</p>	<p>The incidence of vomiting postoperatively usually peaks during the first 4 h after emergence, but the aprepitant group had no reported vomiting episodes during this time frame.</p> <p>This study concludes that the use of aprepitant has an effect on deduction in vomiting incidence along with a delay in time to first vomiting episode in morbidly obese patients.</p>	<p>Level I</p> <p>High quality</p> <p>Limitations: opioid consumption between the two groups was not compared which could have effect emesis</p>
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<p>Vallejo MC, Phelps AL, Ibinson JW, et al., 2012.</p> <p><i>Aprepitant plus ondansetron compared with ondansetron alone in reducing postoperative nausea and vomiting in ambulatory patients undergoing plastic surgery</i></p>	<p>Prospective, double-blinded, randomized, two-arm evaluation study</p>	<p>Sample size: 150 patients</p> <p>Population:</p> <p>Procedure: outpatient plastic surgery</p>	<p>IV1: aprepitant 40 mg</p> <p>IV2: Placebo</p> <p>DV1: ondansetron 4 mg IV</p> <p>Oral aprepitant or placebo was given within 2 hours before the scheduled operation and ondansetron 4 mg IV was given immediately after induction</p>	<p>Verbal rating scores (VRS) were measured over 48 hours after surgery where 0= no nausea, and 10= worst nausea ever</p> <p>Time to vomiting was measured.</p> <p>Nausea and vomiting was recorded by an investigator blinded to treatment group in the preoperative period, on admission to PACU and every hour until the patient was discharged. Patients recorded nausea & vomiting after discharge as well. Patients made diary entries every 4 hours while awake for up to 24 hours after the first day of surgery, and every 8 hours while awake during the second day after surgery (48 hours).</p>	<p>The Kaplan-Meier plot of the hazards of vomiting revealed an increased incidence of emesis in patients receiving ondansetron alone compared to the combination of ondansetron and aprepitant (p=0.006)</p>	<p>The incidence of nausea was not significantly different in the two groups.</p> <p>Severity of nausea was significantly higher in those receiving ondansetron alone, compared to aprepitant + ondansetron as measured by a peak nausea score (p=0.014).</p>	<p>In patients undergoing plastic surgery, use of aprepitant with ondansetron significantly decreases postoperative vomiting rates and nausea severity for up to 48 hours postoperatively .</p>	<p>Level I</p> <p>High Quality</p> <p>Limitations: Rescue treatments were standardized as per institution protocol for postoperative nausea and vomiting, and these treatments may have affected patient outcome. Also, ondansetron was given on induction to ensure that all patients would receive the medication since the duration of the surgeries varied. Most research states that ondansetron has improved efficacy 30 minutes prior to emergence.</p>
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Appendix C: IRB Exemption

Office of Research Integrity
 Research Compliance, MARC 414

MEMORANDUM

To: Dr. Vicente Gonzalez
CC: Alyssa Staubitz
From: Elizabeth Juhasz, Ph.D., IRB Coordinator *EJ*
Date: May 28, 2021
Protocol Title: "An Education Intervention on the Use of Aprepitant versus Ondansetron in the Prevention of Postoperative Nausea and Vomiting (PONV) in Adult Patients Undergoing General Anesthesia"

The Florida International University Office of Research Integrity has reviewed your research study for the use of human subjects and deemed it Exempt via the **Exempt Review** process.

IRB Protocol Exemption #: IRB-21-0193 **IRB Exemption Date:** 05/28/21
TOPAZ Reference #: 110223

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.
- 3) Submit an IRB Exempt Project Completion Report Form when the study is finished or discontinued.

Special Conditions: N/A

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

EJ



Miami Beach Anesthesiology Associates, Inc.

Mount Sinai Medical Center • Division of Anesthesia

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J.P. Mato DNP, CRNA
CRNA Director &
F.U.J. Coordinator
U.M. Coordinator
Berry Unit, Coordinator

Paula Schultz DNP, CRNA
OB-Chief CRNA

March 3, 2021

Fernando C Alfonso, DNP, CRNA, APRN
Assistant Clinical professor
Department of Nurse Anesthetist Practice
Florida International University

Dr. Alfonso,

Thank you for inviting Mount Sinai Medical Center to participate in Doctor of Nursing Practice (DNP) project conducted by Alyssa Staubitz entitled "An Education Intervention on The Use of Aprepitant versus Ondansetron in the Prevention of Postoperative Nausea and Vomiting (PONV) in Adult Patients Undergoing General Anesthesia" in the Nicole Wertheim College of Nursing and Health Sciences, Department of Nurse Anesthetist Practice at Florida International University. I have given the student 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 proposed quality improvement project seeks to investigate and synthesize the latest evidence.

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: Alyssa Staubitz and Dr. Fernando Alfonso.

Once the Institutional Review Board's approval is achieved, this scholarly project's execution will occur over two weeks. Alyssa Staubitz will behave professionally, follow standards of care, and not impede hospital performance. We support the participation of our Anesthesiology providers in this project and look forward to working with you.

Respectfully,

Jampierre (J.P.) Mato, DNP, CRNA, APRN
Executive CRNA Director
SRNA Coordinator/Supervisor
Electronic Mail: Jampierre@bellsouth.net
Mobile Phone: 954-668-6080

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Appendix D: QI Consent**CONSENT TO PARTICIPATE IN A QUALITY IMPROVEMENT PROJECT**

“An Education Intervention on the Use of Aprepitant versus Ondansetron in the Prevention of Postoperative Nausea and Vomiting (PONV) in Adult Patients Undergoing General Anesthesia.”

PURPOSE OF THE PROJECT

You are being asked to be in a quality improvement project. The goal of this project is to increase anesthesia providers’ knowledge on the use and effectiveness of the anti-emetic drug, aprepitant. Through an educational intervention, anesthesia providers will be given the necessary information on how and when utilization of aprepitant can be beneficial in the prevention of postoperative nausea and vomiting in adult patients undergoing general anesthesia.

DURATION OF THE PROJECT

Your participation will require about 20 minutes of your time.

PROCEDURES

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

RISKS AND/OR DISCOMFORTS

There are no foreseeable risks with you for participating in this project.

BENEFITS

The following benefits may be associated with your participation in this project: An increase in cholesterol management knowledge, which will help you to better assess medication adherence and guidelines implementations to reduce the risk of cardiovascular events. The overall objective of the program is to increase the quality of healthcare delivery, improving the health indicator of our patients, and increase patient engagement.

ALTERNATIVES

There are no known alternatives available to you other than not taking part in this project. However, if you 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.

COMPENSATION & COSTS

There is no cost or payment to you for receiving the health education and/or 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 Alyssa Staubitz at 516-241-0306, astau008@fiu.edu or Dr. Fernando Alfonso at 305-348-3510, falfonso@fiu.edu

IRB CONTACT INFORMATION

If you would like to talk with someone about your rights of 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 consent by participating in the survey. I have read the information in this consent form and agree to participate in this project.

Appendix E: QI Project Survey**Pretest and Posttest Questionnaire:****Prevention of Postoperative Nausea and Vomiting (PONV)****INTRODUCTION**

The primary aim of this QI project is to improve anesthesia providers' knowledge on the use and effectiveness of the anti-emetic drug, aprepitant, in order to decrease rates of postoperative nausea and vomiting and improve patient outcomes.

Please answer the question below to the best of your ability. The questions are either in multiple choice or true/false format. These questions are meant to measure knowledge and perceptions on management of postoperative nausea and vomiting, including the use and effectiveness of the neurokinin-1 antagonist, aprepitant.

PERSONAL INFORMATION

1. **Gender:** Male Female Other
2. **Age:** _____
3. **Ethnicity:**
 Hispanic Caucasian African American Asian Other
4. **Position/Title:** _____
5. **Level of Education:** Associates Bachelors Masters Other

6. **Years of experience:** Less than 1 year 1 to 5 6 to 10 more than 10 years

QUESTIONNAIRE

- 1. Postoperative nausea and vomiting (PONV) rates for inpatient surgeries range between:**

- a. 5 - 10 %
- b. 15 – 30 %
- c. 30 – 50 %
- d. 70 – 80%

CORRECT ANSWER: C

- 2. Patients with multiple risk factors experience postoperative nausea and vomiting (PONV) at rates as high as:**

- a. 20 - 30 %
- b. 30 – 40 %
- c. 50 – 60 %
- d. 70 – 80%

CORRECT ANSWER: D

- 3. Complications of PONV include:**

- a. Pulmonary aspiration
- b. Wound dehiscence
- c. Pneumothorax
- d. Unplanned hospital admission
- e. All of the above

CORRECT ANSWER: E

4. Patients have reported that _____ is one of the most concerning possible anesthesia outcomes.

- a. Pain
- b. Vomiting
- c. Nausea
- d. Death

CORRECT ANSWER: B

5. Failure to address PONV as a problem will result in:

- a. Continued patient dissatisfaction with anesthesia
- b. Lengthened post-anesthesia recovery unit (PACU) stays
- c. Increased healthcare costs
- d. All of the above

CORRECT ANSWER: D

6. All of the following are independent risk factors for PONV according to the Apfel scoring system, EXCEPT:

- a. Female gender
- b. Current smoker
- c. History of PONV and/or motion sickness
- d. Use of postoperative opioids.

CORRECT ANSWER: B

7. Patients given antiemetics such as the commonly used 5-HT3 antagonist, ondansetron, still experience PONV _____ of the time.

- a. 5 - 10 %

- b. 10 - 20 %
- c. 30 – 40 %
- d. 40 – 50%

CORRECT ANSWER: C

8. Aprepitant exerts its antiemetic effects via:

- a. Neurokinin-1 receptor antagonism
- b. Serotonin-5-HT₃ receptor antagonism
- c. Dopamine-2 receptor antagonism
- d. Histamine-1 receptor antagonism

CORRECT ANSWER: A

9. All of the following are true of aprepitant EXCEPT:

- a. It has a long half-life of 40 hours.
- b. It is administered orally.
- c. It must be re-dosed every 6 hours.
- d. It is superior to ondansetron in prevention of postoperative vomiting.

CORRECT ANSWER: C

10. Aprepitant's antiemetic effects are

- a. Effective
- b. Somewhat effective
- c. Somewhat ineffective
- d. Most ineffective

11. How likely are you to use aprepitant in the prevention of PONV?


- a. Most likely

- b. Somewhat likely
- c. Somewhat unlikely
- d. Most unlikely

12. How likely are you to recommend aprepitant to other anesthesia providers?

- a. Most likely
- b. Somewhat likely
- c. Somewhat unlikely
- d. Most unlikely

Appendix F: Educational Module




The Use of Aprepitant versus Ondansetron in the Prevention of Postoperative Nausea and Vomiting (PONV) in Adult Patients Undergoing General Anesthesia

BY: ANNEA HARRIS, MD, PhD

Learning Goals

After this educational module, you will:

- Recognize the prevalence of PONV today, despite current advances in healthcare.
- Recognize the significance of addressing the current problem with PONV.
- Understand the mechanism of action of Aprepitant in the prevention of PONV.
- Understand Aprepitant's best use in the prevention of PONV.



Background


PONV along with pain is one of the most common patient complaints associated with major surgery. The long-term cost of patient discomfort is significant.

Major advances in drug therapy have resulted in a reduction in the incidence of PONV in patients undergoing general anesthesia. However, the incidence of PONV remains high, and the incidence of PONV is still a significant problem for patients.

Patients who have PONV are more likely to be readmitted to the hospital, have longer hospital stays, and incur higher costs.


Importance of Addressing the Current Problem of PONV

- High PONV rates contribute to:
 - Patient dissatisfaction with anesthesia
 - Increased PONV morbidity, recovery and quality of life
 - Increased healthcare costs



Complications of PONV

Pulmonary aspiration	Wound dehiscence
Respiratory failure	Admission to intensive care
Postoperative ileus	Delayed discharge



Current Recommendations for Practice

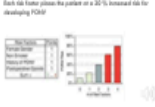
- Identify patients at risk for PONV
- Use prophylactic antiemetic therapy for PONV
- Administer PONV prophylaxis with 1 to 2 interventions for adults at moderate risk
- Administer 2 or 3 interventions for patients at high risk for PONV
- Administer prophylactic therapy to children at increased risk for postoperative vomiting
- Administer ondansetron to patients with PONV who did not receive prophylaxis or to other patients as needed
- Administer PONV prophylaxis to patients in the clinical setting
- Use general multidisciplinary approaches to maximize implementation of PONV policies

Risk Assessment Tool

Apix Risking System
A preoperative risk assessment tool used to identify high-risk patients.


Based on four independent risk factors.

Each risk factor places the patient at a 50% increased risk for developing PONV.




Ondansetron versus Aprepitant

Ondansetron	Aprepitant
• Ondansetron (ZAN) receptor antagonist	• Ondansetron 1 receptor antagonist
• Administered IV	• Administered PO
• Needs to be re-dosed every 8 hours	• Administered once pre-operatively
• Half-life of 3 hours	• Half-life of 11 hours



Study Findings on Aprepitant



Aprepitant provides superior protection against nausea, vomiting, and need for rescue antiemetics compared to ondansetron.

When administered in combination with ondansetron, aprepitant is more effective than administration of ondansetron alone in prevention of postoperative vomiting.

Aprepitant is superior to ondansetron in prevention of postoperative vomiting.

Aprepitant delays time to first vomiting episode.


Mechanism of Action of Aprepitant

Acts in activation of the 5-HT₃ receptor antagonist.

Works primarily in the nucleus tractus solitarius as well as in the nucleus reticularis.

Inhibits the effects of substance P and 5-HT₃ receptors in the brainstem.


Without 5-HT₃ receptors, substance P and 5-HT₃ receptors, vomiting is inhibited.



Aprepitant in the Prevention of Vomiting


Patients who receive aprepitant preoperatively are less likely to be readmitted against vomiting in comparison to those who receive ondansetron.

It has been argued that aprepitant should be administered for PONV prophylaxis specifically in patients at risk for PONV whose vomiting could result in serious complications, such as in patients who require IV or oral therapy.



Recommendations on the Use of Aprepitant

- Aprepitant is superior to ondansetron in prevention of PONV in patients at high risk for PONV or patients with 2 or more risk factors in the adult population.
- Administer aprepitant to patients at risk for serious complications related to postoperative vomiting.
- Administer aprepitant in combination therapy with ondansetron for more effective PONV prophylaxis.
- Aprepitant is superior to ondansetron in prevention of postoperative vomiting in patients at high risk for PONV.



Summary

Evidence suggests that aprepitant, when administered in combination with ondansetron, more effectively reduces the incidence of postoperative vomiting.

A significant advantage of aprepitant is its ability to reduce the incidence of postoperative vomiting.

While aprepitant may be indicated for all patients undergoing general anesthesia, it may have a higher value in the patient at high risk for PONV or in patients at risk for serious effects in the presence of postoperative vomiting.


A combination of aprepitant and ondansetron may be more effective than either drug alone in the prevention of postoperative vomiting.

References

1. American Society of Anesthesiologists. Practice Guidelines for the Management of Postoperative Nausea and Vomiting. Anesthesiology. 2010;72:1-20.
2. Apfel CC, Cook EF, Naguib M, et al. A Practice Guideline for the Prevention of Postoperative Nausea and Vomiting. Anesthesiology. 2012;76:1-15.
3. Apfel CC, Cook EF, Naguib M, et al. A Practice Guideline for the Prevention of Postoperative Nausea and Vomiting. Anesthesiology. 2012;76:1-15.
4. Apfel CC, Cook EF, Naguib M, et al. A Practice Guideline for the Prevention of Postoperative Nausea and Vomiting. Anesthesiology. 2012;76:1-15.
5. Apfel CC, Cook EF, Naguib M, et al. A Practice Guideline for the Prevention of Postoperative Nausea and Vomiting. Anesthesiology. 2012;76:1-15.


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Appendix G: Project Poster



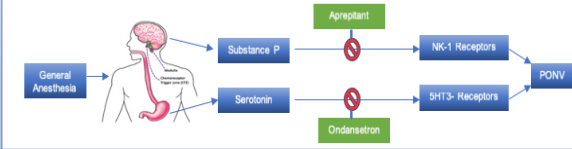
The Use of Aprepitant Versus Ondansetron in the Prevention of Postoperative Nausea and Vomiting (PONV) in Adult Patients Undergoing General Anesthesia

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BACKGROUND

PONV, along with pain, is one of two of the most common patient complaints reported after surgery and is the leading cause of unplanned inpatient admissions.¹ In one study of surgical patients, patients rated vomiting as the number one most concerning possible anesthesia outcome.¹ Despite the increasing number of advances in healthcare, PONV rates remain high.² Aprepitant has demonstrated promising effectiveness in the prevention of PONV and can add value to current healthcare practices.



RESULTS

- Preoperative administration of aprepitant provides superior protection against nausea, vomiting, and need for rescue antiemetics in comparison to ondansetron 4 mg IV.⁸
- Administration of aprepitant in combination with ondansetron is more effective than administration of ondansetron alone in prevention of PONV.^{7,9,10,11}
- Aprepitant is superior to ondansetron in prevention of postoperative vomiting.^{4,5,8}
- Preoperative administration of aprepitant delays time to first vomiting episode.^{4,7,9,10}
- Patients who receive aprepitant preoperatively are two times as likely to be protected against vomiting in comparison to those who receive ondansetron.⁴

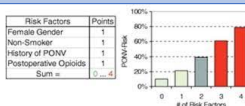
PURPOSE

This systematic review aims to evaluate the current literature on aprepitant regarding its effectiveness in the prevention of PONV. The goal is to determine its effectiveness in comparison to the most commonly used antiemetic, ondansetron.

PICO


(P) In patients 18 years or older undergoing general anesthesia, **(I)** does the administration of aprepitant, including the combination of aprepitant with ondansetron, **(C)** compared to ondansetron alone **(O)** reduce incidence rates of PONV?

RESULTS



CLINICAL SIGNIFICANCE

Incidence rates for inpatient surgeries range between 30% to 50%, with rates as high as 70% to 80% for patients with multiple risk factors.³ Patients given antiemetics such as the commonly used 5-HT3 antagonist, ondansetron, still experience PONV 30% to 40% of the time.⁴ Aprepitant has been approved and shown to be effective for the treatment of chemotherapy-induced nausea and vomiting.⁴ Recently, more studies have been conducted regarding its effectiveness in the treatment and prevention of PONV.



RECOMMENDATIONS FOR PRACTICE

- Administer aprepitant in patients at moderate to high risk for PONV, or in patients with 2 or more risk factors on the Apfel scoring system.
- Administer aprepitant in patients at risk for serious complications related to postoperative vomiting.
- Administer aprepitant as combination therapy with ondansetron for more effective PONV prophylaxis.
- Administer aprepitant no greater than 3 hours prior to induction of anesthesia at a dose of 40 mg PO.

METHODOLOGY

- Research articles were obtained by searching the following databases: PUBMED, CINAHL, & EMBASE.
- **Keywords:** aprepitant, NK-1 antagonist, emend, ondansetron, serotonin 5-HT3 antagonist, and PONV
- **Inclusion criteria:** RCTs, systematic reviews and meta analyses published between 2007-2020, studies measuring aprepitant alone and aprepitant + ondansetron

Literature Review

Author & Year	Design Sample	Major Findings
Diemunsch P, Gan TG, Philip BK, et al., 2007.	RCT	Patients taking aprepitant were two times as likely to be protected against vomiting in comparison to those taking ondansetron. ⁴ Aprepitant delayed time to first vomiting in comparison to ondansetron. ⁴
Gan TJ, Apfel CC, Kovac A, et al., 2007.	RCT	Aprepitant at doses of 40 mg PO and 125 mg PO demonstrated delayed time to first vomiting in comparison to ondansetron alone. ⁵
Singh PM, Borle A, Rewari V, et al., 2016.	Systematic Review and Meta-analysis	Aprepitant showed improved efficacy in prevention against vomiting on post-op days 1 and 2 in comparison to ondansetron. ⁶
Sinha AC, Singh PM, Williams NW, et al., 2014.	RCT	Aprepitant administered with ondansetron showed improved efficacy in prevention of vomiting and time to first vomiting episode in comparison to ondansetron alone. ⁷

REFERENCES

Available upon request. Contact astau008@fiu.edu

**This project was IRB exempt.*