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Effects of Ondansetron 4 Milligrams Compared with Ondansetron 8 Milligrams on the Incidence of Post-Operative Nausea and Vomiting in Patients with Body Mass Index Greater than 30KG/M2 Undergoing Mastectomy

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EFFECTS OF ONDANSETRON 4 MILLIGRAMS COMPARED WITH
ONDANSETRON 8 MILLIGRAMS ON THE INCIDENCE OF POST-OPERATIVE
NAUSEA AND VOMITING IN PATIENTS WITH BODY MASS INDEX GREATER
THAN 30KG/M² UNDERGOING MASTECTOMY

A Research Project submitted to
the Marshall University
Graduate School of Management

Final defense submitted in partial fulfillment
of the requirements for the
Doctorate of Management Practice in Nurse Anesthesia (DMPNA) degree
conferred by Marshall University (MU) in partnership with the
Charleston Area Medical Center (CAMC) based on a collaborative agreement between
the MU Lewis College of Business and the CAMC School of Nurse Anesthesia

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EXECUTIVE SUMMARY

Introduction: Post-Operative Nausea and Vomiting (PONV) is a recurrent and frequent issue for the patient, the anesthesia team, and Post Anesthesia Care Unit (PACU) team. Both pharmacologic and non-pharmacologic recommended modalities have been utilized for both the prevention and treatment of PONV in the surgical-anesthesia setting. The 5-HT₃-receptor antagonist ondansetron is one of the many known pharmacological modalities commonly utilized by anesthesia providers in preventing PONV.

Methodology: The design used for this research was a quantitative, retrospective case control study that evaluated existing data enclosed in the Electronic Medical Records (EMR) from Charleston Area Medical Center (CAMC), which is made up of four hospitals. The sample population included 89 patients: 64 patients with a BMI $\geq 30\text{kg/m}^2$ who have received ondansetron 4 milligrams (mgs) and 25 patients with a BMI $\geq 30\text{kg/m}^2$ who have received ondansetron 8 mgs. In this sample population, all of the patients were 18 to 64 years of age with an American Society of Anesthesiologist (ASA) I-IV undergoing mastectomy.

Results: There were no statistical significance found between the ondansetron dosage and the occurrence of PONV. There were no statistical significance found between the two groups and BMI ($p > .05$). The mean BMI for ondansetron 4 mgs group was 37kg/m^2 and ondansetron 8 mgs group was also 37kg/m^2 . The mean dose of rescue antiemetic received in the PACU also did not show to be statistically significant between the two groups ($p > .05$).

Discussion: Approximately 19% of the patients in this study experienced PONV despite the intra-operative administration of ondansetron. There were no statistical significance that was found between the ondansetron dosing and PONV. This may be the result that the dosing of ondansetron may truly not make a difference in preventing PONV.

Conclusion: The outcome of this study did not express any statistically significant difference in the 4 mgs and 8 mgs dosing of ondansetron and the occurrence of PONV or the amount of rescue anti-emetic received in PACU.

Practical Implications: The result of this study did not demonstrate any additional benefit from a larger dose of 8 mgs compared to a dose of 4 mgs of ondansetron. Dosing 4 mgs may just be as effective as 8 mgs, which simply brings to light that more is not simply better in all cases. Further research is needed on this topic.

Key Words: Post-operative nausea and vomiting, ondansetron, mastectomy, body mass index, rescue anti-emetic.

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INTRODUCTION

Background and Significance of the Problem

Post-Operative Nausea and Vomiting (PONV) is a recurrent and frequent issue for the patient, the anesthesia team, and Post Anesthesia Care Unit (PACU) team. Both pharmacologic and non-pharmacologic recommended methods have been utilized for both the prevention and treatment of PONV in the surgical-anesthesia setting. The most common and distressing symptoms that follow surgery with the utilization of anesthesia include both emesis and pain (Gupta, Wakhloo, Lahori, Mahajan, & Gupta, 2007). Prevention and treatment of PONV in surgical procedures that are highly associated with this risk is usually at the discretion of the anesthesia provider of what they think is the best regimen for that patient type.

The adverse effects of PONV range from patient related distress to post-operative life threatening morbidities (Smith, Smith, & Smith, 2012). Patients are willing to tolerate pain with a higher degree to that of PONV and often rate PONV as worse than post-operative pain (Gan, 2002). It is not surprising that the prevention of PONV improves patient satisfaction by those who are highly at risk for it (Darkow, Gora-Harper, Goulson, & Record, 2001). Patients were willing to pay United States (US) \$56 for an antiemetic that would completely prevent PONV and those who developed PONV, were willing to pay US \$73 and \$100 respectively (Gan, Sloan, de L Dear, El-Moalem, & Lubarsky, 2001).

Patients with no known risk factors carry a 10% risk of PONV, and this risk increases drastically to 61% and 79% respectively, when 3 or 4 risk factors exists (female gender, nonsmoker, history of motion sickness, post-operative opioid use, and a history

of PONV) (Roberts, Bezinover, & Janicki, 2012). Despite the existence of various tools to categorize those at risk for developing PONV and implementing multiple PONV prevention and treatment regimens, clinicians do not appear to methodically address these issues in an identical approach that utilizes both non-pharmacologic and pharmacologic modalities to minimize PONV (Smith et al., 2012). The research on PONV is vast and since it is so common, both the prevention and treatment modalities can range from non-pharmacological to pharmacological, or both.

Literature Review

Nausea and vomiting are amongst the most common post-operative disorders that can occur with various types of anesthesia. The term nausea and vomiting are intertwined, but yet these remain two separate entities and should be evaluated individually. Nausea is defined as a subjective unpleasant sensation in which the patient is aware of the desire to expel gastric contents, but does not necessarily do. Vomiting is expressed as the expulsion of gastric contents orally by the physical motion of the contraction of the abdominal muscles, descent of the diaphragm, and opening of the gastric cardia (Golembiewski, Chernin, & Chopra, 2005).

Because of the physical and emotional stressors of PONV, these consequences can be seen as life –menacing to the patient. Preventing PONV improves satisfaction scores among those patients who are at an increased risk of experiencing them (Darkow et al., 2001). Patients report the avoidance of pain is far less a concern than that of PONV and although rarely fatal, it can be uncomfortable and be associated with dissatisfaction with their peri-operative care (Rahmann & Beattie, 2004). Some of these physical consequences of PONV include sweating, pallor, tachycardia, stomachache,

increased risk of esophageal rupture, wound dehiscence, and electrolyte imbalance (Gupta et al., 2007). Multiple physical characteristics related with PONV may be mild, but the impact on patients and their recovery can be much more severe. Some of these complications include the inability to mobilize after surgery, restricted oral intake, delayed recovery, and delayed discharge after surgery (Gan et al., 2007).

There are many risk factors and contributing factors that increase or add to the effects of PONV. Pre-operative dehydration may occur due to the fact that pre-operative orders usually include directions to remain nothing-by-mouth (NPO), and can affect post-operative consequences. Because of this NPO status, gut hypoperfusion may occur and is identified as one of the contributing factors to PONV. To assist with mesenteric perfusion, likely to prevent PONV, preloading with large volumes of fluids is usually administered by anesthesia prior to induction (Chaudhary, Sethi, Motiani, & Adatia, 2008). Post-operative patients can have outcomes such as thirst, dizziness, and drowsiness, and nausea may be predisposed by the little to none patient's fluid status intake before and after surgery. The use of opioids in any phase of the surgery can produce nausea and vomiting by direct stimulation of the chemoreceptor trigger zone (CTZ), induced delayed gastric emptying, and decreased gastric motility (Bailey, Egan, & Stanley, 2000).

There are PONV scales available to determine risk factors and or the severity of PONV in the post-operative phase, which include the Apfel score and the Visual Analogue Scale (VAS). The Apfel score considers four risk factors: the female gender, previous history of PONV or motion sickness, non-smoking status, and post-operative use of opioids (Pierre, Benais, & Pouymayou, 2002). Severity of nausea and vomiting is

assessed by the (VAS): Score 0- no nausea or vomiting, Score 1- nausea, Score 2- retching or mild vomiting, Score 3- two or more vomiting(s) in a 30 minute duration (Gupta, & Jain, 2014).

PONV is a common complication that patients experience following breast surgery (Watwill et al., 2003). The stated occurrence of PONV in patients undergoing breast surgery with axillary dissection is about 60-80% (Fujii, 2006). The pharmacologic drugs, which include 5-HT₃ receptor antagonists, are widely used drugs given routinely by anesthesia providers as a first line modality in the prevention of PONV. Because breast surgery is commonly associated with PONV, the modalities to help prevent and or treat PONV are comprised of multimodal therapies that utilize both non-pharmacological and pharmacological programs.

Many modalities to prevent and treat PONV have been utilized by anesthesia in recent decades. Some non-pharmacologic and alternative techniques for the prevention and treatment of PONV include, but are not limited to, acupuncture, electro-acupuncture, acupoint stimulation, acupressure, transcutaneous nerve stimulation, ginger, hypnosis, and aromatherapy (Golembiewski, et al., 2005). The most commonly used method to treat severe PONV is the administration of an intravenous (IV) anti-emetic agent that obstruct emetogenic neurotransmitters (NT) at the level of the CTZ located within the brain. Some of these NT include serotonin (5-HT₃), dopamine, histamine, and acetylcholine. The introduction of 5-HT₃ receptor antagonists was a major breakthrough in the 1990's and represented a major development in pharmacotherapy in regards to treatment regimens that induced nausea and vomiting (Radford, Fuller, Bushey, Daniel, & Pellegrini, 2011). Ondansetron was the first drug to be introduced and is the most

commonly used drug in the class of 5-HT₃ receptor antagonists (Ku, & Ong, 2003). According to Golembiewski et al. (2005), the recommended dose for ondansetron in an adult is 4 milligrams (mgs), but Ku and Ong state that the optimal prophylactic intravenous dose of ondansetron is 8 mgs for long-term efficacy (Ku & Ong, 2003). The clinical side effect of the drug ondansetron includes the commonly reported headache and the ability to prolong the QT interval on the electrocardiogram (Butterworth, Mackey, Wasnick, Morgan, & Mikhail, 2013). For these reasons, the clinician administering the drug must be vigilant in understanding the pharmacodynamics and clinical side effects of ondansetron.

In this study, the researcher planned to investigate a common prophylactic prevention and treatment of PONV utilized at Charleston Area Medical Center (CAMC) to determine if there was a decrease in the occurrence of PONV.

Statement of the Problem and Research Purpose

PONV is a common issue at CAMC, and because there are a multitude of prevention and treatment regimens among varying anesthesia providers, an investigation of a commonly utilized prophylactic treatment was complete. A mutual practice at CAMC is the administration of ondansetron 8 mgs in obese patients instead of the standard dose of ondansetron 4 mgs.

The purpose of this retrospective investigation is to determine if patients with a BMI $\geq 30\text{kg/m}^2$ undergoing mastectomy procedure, who have received ondansetron 4 mgs intra-operatively, experienced more PONV than those who have received ondansetron 8 mgs.

Another purpose of this investigation is to determine if obese patients with a BMI $\geq 30\text{kg/m}^2$ who experienced PONV after receiving ondansetron 4 mgs intra-operatively, required more rescue anti-emetic medication than those who received ondansetron 8 mgs.

If this is so, facilities can possibly implement the use of 4 mgs of ondansetron instead of 8 mgs on patients with a BMI $\geq 30\text{kg/m}^2$ undergoing mastectomy, and can reduce the costs associated with the assumption that BMI's $\geq 30\text{kg/m}^2$ require more pharmacological interventions. By utilizing the minimal amount of ondansetron, needed to prevent PONV, can this also reduce the associated side effects seen with ondansetron?

METHODOLOGY

Research Hypothesis

This retrospective study was analyzed using the hypotheses: 1) In a group of ASA I-IV adult patients with a BMI $\geq 30\text{kg/m}^2$ undergoing a mastectomy procedure who received 4 mgs of ondansetron, there will be fewer incidences of PONV than those who received 8 mgs. 2) In a group of ASA I-IV adult patients with a BMI $\geq 30\text{kg/m}^2$ undergoing a mastectomy procedure that received 4 mgs of ondansetron will require less amounts of rescue anti-emetic given than those who received 8 mgs.

Research Design and Setting

The design used for this research was a quantitative, retrospective case control study evaluating existing data enclosed in the Electronic Medical Records (EMR) from Charleston Area Medical Center (CAMC), which is made up of four hospitals.

Sample Population with Description

The sample population used for this retrospective study included female patients who underwent a unilateral simple mastectomy and bilateral simple mastectomy at CAMC Health System between January 1, 2005 and June 1, 2015. Males in this study were excluded due to only 10 males or 2 percent out of 363 charts were analyzed and only 3 males or 30 percent of all males made the inclusion criteria. The sample included 64 patients ages 18-64, measured in years, with a BMI greater than or equal to 30 kg/m² who received ondansetron 4 mgs and 25 patients with a BMI greater than or equal to 30 kg/m² who have received ondansetron 8 mgs. The patients were identified using the following ICD10 procedure code: 85.41 unilateral simple mastectomy and 85.42 bilateral simple mastectomy.

Inclusion Criteria:

1. Adult patients 18 to 64 years of age.
2. Patients with American Society of Anesthesiologists (ASA) physical status I-IV.
3. Patients who underwent general anesthesia for mastectomy with a BMI greater than or equal to 30 kg/m² and received either ondansetron 4 mgs or ondansetron 8 mgs.

Exclusion Criteria:

1. Patients that have a history of PONV.
2. Patients that have a history of a gastrointestinal (GI) disorders such as Crohn's disease, Ulcerative Colitis (UC) or Irritable Bowel Syndrome (IBS).

3. Patients that received any other anti-emetic or medications that are known to have anti-emetic properties (i.e. Benadryl).
4. Patients 17 years of age and younger or 65 years of age and older.
5. Patients with an ASA physical status V-VI.
6. Patients who underwent general anesthesia for mastectomy with a BMI less than 30 kg/m² and received either ondansetron 4 mgs or ondansetron 8 mgs.

Procedure and Protocol

A retrospective chart review was completed on patient records that have undergone mastectomy at CAMC Health System from January 1, 2005 to June 1, 2015. To test the hypothesis, the following variables were collected: ondansetron dosage (4 mg versus 8 mg), BMI, occurrence of PONV, amount of rescue anti-emetic for PONV in the PACU, age, gender, and ASA status. BMI is defined as a numeric calculation based on the patient's weight and height for evaluation of patient's body fatness for most people (CDC, 2015). Nausea is defined as a subjective unpleasant sensation in which the patient is aware of the desire to expel gastric contents, but does not necessarily do. Vomiting is expressed as the expulsion of gastric contents orally by the physical motion of the contraction of the abdominal muscles, descent of the diaphragm, and opening of the gastric cardia. Obesity is identified as a BMI greater than or equal to 30kg/m² and a BMI of greater than or equal to 30kg/m², is to be considered obese for this study (CDC, 2015). The utilization of rescue anti-emetic(s) is to be associated as a pharmacological agent(s) used for the treatment of PONV. Age is to be labeled as 18 to 64 years. Gender is to be classified as male or female. Physical health status of each patient will be determined using ASA numerical scale from I-VI (ASA, 2015). For the purpose of this study,

patients with a physical status of I-IV are to be incorporated. The ASA classifications are:

1. A normal healthy patient.
2. A patient with mild systemic disease.
3. A patient with severe systemic disease.
4. A patient with severe systemic diseases that is a constant threat to life.

Data Collection and Instruments

Data collection was conducted by using existing data from each patient's individual EMR. Each patient was given a number in the order in which the data was collected and the number in no way linked the data collected to the patient it belonged to. Individual data used was collected from the pre-operative anesthesia assessment flow sheet, anesthesia record, and the PACU patient documentation sheet.

Detailed data used was collected from the pre-anesthesia evaluation, anesthesia record and the PACU patient documentation during the patient's time in the recovery phase at CAMC Health System. The anesthesia record flow sheet used on each patient undergoing anesthesia at CAMC contained enclosed information including: surgical procedure, significant times in the operating room, medications administered, vital trends, and other patients' surgical data. The PACU at CAMC General, Memorial, Woman and Children's, and Teays Valley hospitals cares for the patient's needs immediately after surgery until patients have stabilized and are able to be transferred to a nursing floor or discharged home.

The PACU flow sheet was used to record patient data during the time that the patient was in the recovery room after surgery. The PACU flow sheet enclosed material

that was collected for the study including: the occurrence of nausea and vomiting and the dosages of the rescue anti-emetic administered.

Data collection worksheets were established to aid in collection and organization of patient data. Data Collection Worksheet 1 was used to assign each patient a study participant number that was linked to each patient's identification number in order to protect patient identity (Appendix A). Data Collection Worksheet 2 served to organize data for gender, age, height, weight, ASA, ondansetron dosage intra-operatively, occurrence of PONV, amount and usage of rescue antiemetic (Appendix B). All data collected were recorded using these two data collection tools designed by the researcher for this study.

Statistical Design and Analysis

The purpose of this study was to determine if patients with a BMI $\geq 30\text{kg/m}^2$ undergoing mastectomy procedure, who have received ondansetron 4 mgs intra-operatively, experienced more PONV than those who have received ondansetron 8 mgs. Another purpose of this investigation was to determine if obese patients with a BMI $\geq 30\text{kg/m}^2$ who experienced PONV after receiving ondansetron 4 mgs intra-operatively, required more rescue anti-emetic medication than those who received ondansetron 8 mgs. Independent variables in this study included: age, BMI, ASA physical status, and ondansetron dosage. Dependent variables analyzed were: PONV and dosage of rescue antiemetic required for relief of PONV.

The Pearson Chi-square was used to determine if there was a statistical significant difference between the ondansetron dosing groups with regards to physical status. The Fisher's exact test was used to assess the statistical significance

of the occurrence of PONV and ondansetron dosing of 4 mgs and 8 mgs.

A student t-test was used to determine if there was a statistical significant association between the two groups in regards to age and BMI. A student t-test was used to determine the difference between the mean doses of ondansetron and promethazine received in the PACU between both groups. A logistical regression was used to determine if there was a relationship between ondansetron dosage intra-operative and the occurrence of PONV, age, BMI, and ASA. The logistical regression was again used to determine if there was an association between the rescue anti-emetic dose of promethazine and ondansetron and the intra-operative dose of ondansetron, age BMI, and ASA. The level of statistical significance was set at $p < .05$.

Ethical Considerations

This study was approved by CAMC and West Virginia University/Charleston Division Institutional Review Board on September 1, 2015 (Appendix C).

RESULTS

The mean age of all patients was 53 years with 100% of the population being female. From a total of 89 patients that were included in the study, 71% of patients received ondansetron 4 mgs dosing intra-operatively (ondansetron 4 mgs group) and 28% of patients received ondansetron 8 mgs dosing intra-operatively (ondansetron 8 mgs group), (Table 1). The independent samples t-test did not show a statistically significant difference between the mean age between ondansetron 4 mgs and ondansetron 8 mgs groups ($p > .05$),

The mean BMI for all patients was 37 kg/m². The mean BMI of patients receiving ondansetron 4 mgs was 37 kg/m² while the mean BMI of patients receiving

ondansetron 8 mgs was also 37 kg/m². The independent samples T-test did not show a statistically significant difference between the mean BMI between ondansetron 4 mgs and ondansetron 8 mgs groups (p >.05), (Table1).

Most of the total patients in the study were ASA status II and III classifications (Table 1). Thirty- four percent of the total patients in the study were ASA I and II classifications, with 32% receiving ondansetron 4 mgs and 40 % receiving ondansetron 8 mgs. Fifty-eight of the total patients in the study were ASA III and IV classification, with 67% receiving ondansetron 4 mgs and 60% receiving ondansetron 8 mgs (Table 1). The Pearson Chi-square test did not show a statistically significant difference between the ASA status between ondansetron 4 mgs and ondansetron 8 mgs groups (p >.05), (Table1).

Table 1: Clinical Characteristics of Female Patients Undergoing Mastectomy Receiving Intraoperative Ondansetron 4 milligrams and Ondansetron 8 milligrams

Variable	Total (N= 89)	Ondansetron 4mgs (N=64)	Ondansetron 8mgs (N=25)	P- Value
Age (years)				
Mean Age	53	53	52	NS ^T
Gender				
Female	89 (100)	64 (100%)	25 (100%)	NS ^{TT}
BMI (kg/m ²)				
Mean BMI	37	37	37	NS ^T
ASA Physical Status Classification				
I & II	31 (34%)	21 (32%)	10 (40%)	NS ^{TT}
III & IV	58 (65%)	43 (67%)	15 (60%)	NS ^{TT}

*Indicates Statistical Significance at p < .05, NS = Not Significant, kg/m²=kilograms per meters squared. Fisher's Exact not completed for cells less than 5. ^T Indicates T-test

^{TT} Indicates Pearson Chi-square test

Seventeen total patients experienced PONV in the study (Table 2). Twenty- three percent of patients who received ondansetron 4 mgs intra-operatively experienced PONV compared to 8% of patients who received 8 mgs ondansetron intra-operatively (Table 2). The difference in the occurrence of PONV between the patients who received ondansetron 4 mgs and ondansetron 8 mgs intra-operatively was not found to be statistically significant ($p >.05$), (Table 2).

Table 2: Comparison Between Patients Receiving Ondansetron 4 milligrams and Ondansetron 8 milligrams and Occurrence of Post-operative Nausea and Vomiting Utilizing the Fisher’s Exact Test

Variable	Total (N = 89)	Ondansetron 4 mgs (N = 64)	Ondansetron 8 mgs (N = 25)	P- Value
Occurrence of PONV				
Yes	17 (19%)	15 (23%)	2 (8%)	NS
No	72 (80%)	49 (76%)	23 (92%)	

*Indicates Statistical Significance at $p < .05$, NS = Not Significant, PONV = Post operative Nausea and Vomiting, mgs = milligrams

Seventeen total patients in the study experienced PONV and most received a rescue anti-emetic (Table 3 a). Fifteen of these patients were in the ondansetron 4 mgs group and received an average dose of 4.16 mgs of promethazine (Table 3 a). Two whom experienced PONV were in the ondansetron 8 mgs group and received an average dose of about 1.68 mgs of promethazine (Table 3 a). In a t-test comparison, there were no statistically significant differences in the dosing of promethazine rescue anti-emetic between these groups ($p >.05$), (Table 3 a).

Table 3 a: A T-test Measuring Association Between Dosing of Promethazine for Rescue Anti-emetic in Post-Anesthesia Care Unit Between Patients Receiving Ondansetron 4 milligrams and Ondansetron 8 milligrams

Variable	Total (N = 17)	Promethazine dose (mgs), Mean	Std. Deviation	P-Value
Intra-operative Ondansetron dosing				
4 mgs	15	4.16	4.5	NS
8 mgs	2	1.68	2.3	

*Indicates Statistical Significance at $p < .05$, NS = Not Significant, mgs = milligrams

Seventeen total patients in the study experienced PONV and received rescue antiemetic (Table 3 b). Fifteen of these patients were in the ondansetron 4 mgs group and received an average dose of 1.86 mgs of ondansetron in the PACU (Table 3 b). Two whom experienced PONV were in the ondansetron 8 mgs group and received an average dose of 0 mgs of ondansetron in the PACU (Table 3 b).

Table 3 b: A T-test Measuring Association Between Dosing of Ondansetron for Rescue Anti-emetic in Post-Anesthesia Care Unit Between Patients Receiving Ondansetron 4 milligrams and Ondansetron 8 milligrams

Variable	Total (N = 17)	Ondansetron dose (mgs), Mean
Intra-operative Ondansetron dosing		
4 mg	15	1.86
8 mg	2	0

The Binary Logistic Regression analysis showed that there were no statistical significant associations between PONV and those who received rescue anti-emetic, and

the rest of the variables: age, BMI, ASA, ondansetron intra-operative dose ($p > .05$),

(Table 4).

Table 4: Using Binary Logistic Regression for Post –Operative Nausea and Vomiting in Females Undergoing Mastectomy Receiving Rescue Anti-emetic Analysis

Step 1	B	S.E	Wald	df	Sig.	Exp (B)	Sig. (2-tailed)	95% Confidence Interval of the Difference (Upper)	P-Value
Age (years)	-.030	.036	.722	1	.395	.970	.415	5.2659	NS
BMI (kg/m ²)	-.034	.047	.505	1	.477	.967	.937	3.0487	NS
ASA	.368	.549	.450	1	.502	1.445	-	-	NS
Ondansetron dose in mgs	.314	.201	2.429	1	.119	.731	-	-	NS
Constant	2.002	2.963	.457	1	.499	7.404	-	-	NS
Rescue drug Promethazine in mgs	-	-	-	-	-	-	.139	1.9674	NS
Rescue drug Ondansetron in mgs	-	-	-	-	-	-	.087	.93945	NS

Indicates Statistical Significance at $p < .05$, kg/m²=kilograms per meters squared, mgs = milligrams, (-) = no value indicated, NS= Not Significant

The Binary Logistic Regression analysis showed that there were no statistical significant association between PONV and the rest of the variables: age, BMI, or ondansetron intra-operative dose ($p > .05$), (Table 5).

Table 5: Using Binary Logistic Regression for Post –Operative Nausea and Vomiting in Females Undergoing Mastectomy Analysis

	B	95% Confidence Interval of the Difference (Upper)	P-Value
(Constant)	2.002	-	NS
Age (years)	-.030	5.2659	NS
BMI (kg/m ²)	-.034	3.0487	NS
Ondansetron 4 mgs Ondansetron 8 mgs	-.314	-	NS

* Indicates Statistical Significance at $p < .05$, NS = Not Significant, kg/m²=kilograms per meters squared, mgs = milligrams, (-) = no value indicated

DISCUSSION

Discussion of Study Results

Despite all of the female patients in this study receiving an intra-operative dosing of ondansetron, about 19% still experienced PONV and is consistent with current literature that being a female is a risk factor that increases the risk for PONV (Eberhart, et al., 2004). The independent samples T-test did not show a statistically significant difference association between the mean age and BMI between ondansetron 4 mgs and ondansetron 8 mgs groups. The Pearson Chi-square test did not show a statistically significant difference in association between the ASA physical status and ondansetron 4 mgs and ondansetron 8 mgs groups. Literature studies correlate that the BMI and ASA physical status is not a significant predictor of PONV, but according to the Apfel risk

model for the probability of PONV, female gender, non-smoking, history of PONV, and the use of post-operative opioids are (Choi, Ko, Ahn, & Kim, 2005).

The Fisher's exact test was used to determine if there was an association between ondansetron dosing and the occurrence of PONV, but there was no statistical significance. Per existing literature, ondansetron is recommended to be given at the end of the case and not at the start of it, and some of the patients were noted to have an intra-operative dose at the start of the case, which may contribute to why some patients still developed PONV despite receiving a dose of intra-operative ondansetron (Quaynor & Raeder, 2002). Another plausibility concluding that there was no statistical significance association between dosing and PONV may have been that 8 mgs of ondansetron offers no greater efficacy than 4 mgs intravenously as evidenced by standing literature (Golembiewski, Chernin, & Chopra, 2005). In this instance, more of ondansetron may not simply mean there will be a lesser chance of PONV.

There was no statistically significance found between the intra-operative ondansetron dosing groups and the mean doses of rescue anti-emetics (promethazine/ondansetron) received in the PACU utilizing the T-test formula. This could perhaps be expounded by other treatment modalities performed by the PACU team such as intravenous fluids, application of supplemental oxygen, or treatment of a low blood pressure, which can contribute to nausea and vomiting. Existing literature states that non-pharmacological modalities such as hydration and maintaining blood pressure have been shown to be effective in treating and preventing PONV (Golembiewski & O'Brien, 2002).

The result of the binary logistical regression analysis showed that there was not a statistical significant association between PONV and the rest of the variables: age, BMI, or ondansetron dosing. As evidenced by literature studies, there may be no association between PONV and the variables age and BMI, suggesting that ondansetron dosing may not make a difference in the occurrence of PONV (Jaffe, Campbell, Bellman, & Baildam, 2000).

The outcome of the binary logistical regression analysis showed that there was not a statistical significant association between the administration of rescue anti-emetic dosing and the rest of the variables: age, ASA, BMI, or intra-operative ondansetron administration. A multi-modal approach to decrease PONV involves the utilization of both pharmacological and non-pharmacological prophylaxis to reduce the baseline risk such as hydration, oxygen, and blood pressure support, which is a continuation modality in the PACU setting where the rescue anti-emetic dose would be administered (Gan et al., 2007). This may suggest that the dosing of the rescue anti-emetic when PONV is present had no association with the intra-operative dosing of ondansetron, age, ASA, or BMI.

Study Limitations

A limitation to this retrospective study would consist that this may not provide definite information about the cause-and-effect relationship. A more causal type of design would consist of a longitudinal study, which is observational like the cross-sectional design, except these studies extend beyond a single moment and can establish sequence of events (IWH, 2015). Errors and omissions can result in poor documentation and or misinterpretation of data, especially in a retrospective study.

A total of 363 charts were analyzed due to only 363 patients were coded for the two ICD 10 codes of 85.41 and 85.42. between January 1, 2005 to June 1, 2015, and only 89 charts or 24% of them met the inclusion criteria requirements. Out of the 363 charts, only 10 were male or 2%, and because of a small percentage that made the inclusion criteria, there were not any male patients that were included in the study. Mastectomies in males, for the treatment of breast cancer, is rare due to the disease in males is uncommon and accounts for only one percent of all breast cancers diagnosed in the world wide annually (Korde et al., 2010).

Another limitation in this study includes a skewed amount of ondansetron given in which 71% of the patients received 4 mgs and only 28% received 8 mgs in the 89 patients that were part of the inclusion criteria. This may have been due to provider preference due to caution taken with higher doses as to minimize the side-effect associated with ondansetron, which most commonly is that of a QT interval prolongation on an electrocardiogram reading (Kator, & Kim, 2015).

When assessing all 89 charts, there was not a single patient that received more than 8 mgs of ondansetron, including the pre-operative, intraoperative, and postoperative periods, and this may be associated with that 8 mgs may be the maximum one feels comfortable giving because of the unwanted side-effects or they may assume it is not effective and or switch to another anti-emetic. According to the US Food and Drug Administration (FDA), an update in 2012 states that GlaxoSmithKline (GSK) has announced changes to the label of the drug Zofran or ondansetron, stating its use in adults and children with chemotherapy-induced nausea and vomiting at the lower intravenous dose recommended in the drug label, a dose of 0.15 mg/kg administered every 4 hours for

three doses. High doses of ondansetron, such as 32 mgs in a single intravenous administration may affect the electrical activity of the heart and can pre-dispose the patient to abnormal or potentially fatal heart rhythms (FDA, 2011). Because of the risk of pre-disposing patients to unwarranted side-effects associated with higher dosages of ondansetron within the perioperative period, of those patients who received 8 mgs intraoperative, they were not given an additional dose of ondansetron as a rescue anti-emetic in PACU and instead promethazine was given, causing the data to be skewed with zero patients receiving ondansetron.

An additional limitation could have been poor documentation on the PACU flow sheet was a common trend noticed, possibly related to charting in 15 minutes increments such as inconsistencies with anti-emetic given, but there was no indication of PONV. Poor quality or missing information may significantly affect the results of a retrospective statistical investigation (Braaf, Manias, Riley, 2011).

Additional treatment modalities in the anesthesia-surgical setting and or PACU may have helped with the prevention and or treatment of PONV including but not limited to, anxiolytic administration, low-dose of neuromuscular blocking drug such as neostigmine, which in high-doses can cause PONV, and adequate intravenous fluid resuscitation of crystalloids and colloids (Chandrakantan, & Glass, 2011). These influences were not examined as part of this study, which thereby could amend the results.

CONCLUSION

There was not any statistically significant difference in the 4 mgs and 8 mgs dosing of ondansetron and the occurrence of PONV or the amount of rescue anti-emetic received in

PACU. In this study, 4 mgs ondansetron intra-operatively dosing was associated with the same prevention of PONV and utilization of rescue anti-emetics compared to the 8 mgs dosing of ondansetron.

IMPLICATIONS AND RECOMMENDATIONS

Prevention of PONV is crucial for both the patient's safety and satisfaction enduring any surgical procedure. Multimodal prevention and treatment modalities are at the discretion of the anesthesia provider, and the norm of the environment may also affect their choices. Dosing 4 mgs may just be as effective as 8 mgs, which simply brings to light that more is not simply better in all cases. The results of this study can allow for a more cost-effective treatment plan when utilizing the drug ondansetron resulting in cost savings for both the facility and patient, and decrease associated side effects seen with higher dosing of ondansetron. The study of this research may contribute to the anesthesia providers in planning appropriately for each individual patient in the prevention of PONV. Further research is needed on this topic.

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APPENDIX C:



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