

Review

# Efficacy of Antiemetic Drugs in Preventing Nausea and Vomiting in Patients Undergoing General Anesthesia: A Systematic Review

George Warda, M.D.<sup>1</sup>

<sup>1</sup> Georgetown University Medical Center

Keywords: Postoperative nausea and vomiting (PONV), Antiemetic, ramosetron, dexamethasone, droperidol, tropisetron), ondansetron <a href="https://doi.org/10.62186/001c.120231">https://doi.org/10.62186/001c.120231</a>

# Academic Medicine & Surgery

#### Introduction

Postoperative nausea and vomiting (PONV) is a persistent clinical problem among many anesthetic patients who have undergone surgical operations. Approximately 20-50% of surgical patients develop PONV, which rises to about 80% for patients considered at high risk. Although antiemetic drugs have been widely accepted for treating PONV, conducting a systematic analysis to examine their efficacy to guide clinical decisions and enhance patient outcomes is critical.

#### **Methods**

This study employed a systematic review design. The information investigating the efficacy of antiemetic drugs was retrieved from various databases, including PubMed, Cochrane Library, and Google Scholar. Only cohort studies and randomized controlled trials (RCTs) published in English and conducted within the last five years were included.

#### Results

A pooled analysis of the six studies showed that PONV incidence for the experimental group was (OR 0.37, 95% CI: 0.28:0.40, P <.05). Most studies reported a significant drop in severe clinical symptoms, including nausea and vomiting after taking antiemetic drugs.

# Conclusion

Most antiemetic drugs are effective in reducing the incidence of PONV. However, the efficacy varies from one medication to another, calling healthcare practitioners to be more diligent when treating severe forms of PONV.

## 1.0. INTRODUCTION

# 1.1. BACKGROUND

Postoperative nausea and vomiting (PONV) is a common condition among anesthetic patients, manifested clinically by nausea, vomiting, and retching in the first 24 hours after surgery. It is a frequent postoperative complication with debilitating impacts, such as excruciating pain that lowers patient satisfaction and extends patient's stay at the hospital. The severe effects associated with the PONV lead to unplanned readmissions that place a significant financial burden on the family members. In addition to these negative effects, Unsal et al. posited that PONV may result in other problems, including higher medication costs, severe bleeding, aspiration pneumonia and electrolyte imbalance.<sup>2</sup> Countermeasures to control and manage postoperative nausea and vomiting following general anesthesia are fundamental to promoting high-quality recovery and patient satisfaction after surgery.

Although the world has made considerable efforts to reduce anesthesia-related nausea and vomiting, such as using antiemetic drugs or implementing non-pharmacolog-

ical interventions, PONV's prevalence among the general population remains extremely high. About 75 million patients receive anesthesia worldwide each year, with an estimated 33% developing PONV. Teshome et al. found that around 20-50% of anesthetic patients develop PONV, and this prevalence increases dramatically to 80% among patients with high-risk factors such as, the type and duration of surgery, age, sex, prior history of PONV, smoking status, history of motion sickness, etc.4 These findings were justified by Chen and Chang, who reported that PONV is the most common postoperative condition.<sup>5</sup> For patients who have undergone craniotomy, the incidence rate of PONV can rise to 50% and 80% for patients with high-risk factors.5 Qian et al. found that female gender, the presence of postoperative pain, and an operation time greater than one hour substantially increase the incidence of PONV after an ambulatory surgery.6 Hence, reducing postoperative pain, as well as operation time, are fundamental methods of reducing PONV following an outpatient surgical operation. Even though antiemetic drugs are widely accepted in managing and preventing PONV, their effectiveness differs due to different factors as outlined above, emphasizing the need for a systematic review to guide clinical decisions and enhance patient outcomes.

#### 1.2. OBJECTIVE

- To demonstrate the efficacy of antiemetic drugs in managing and controlling PONV complications after surgery.
- 2. To compare the efficiency of existing antiemetic medications in managing PONV complications following a surgery.

#### 2.0. METHODS

## 2.1. PROTOCOL AND REGISTRATION

The research was conducted according to PRISMA guidelines.<sup>7</sup> The study adheres to the systematic literature review (SLR) protocol introduced by Kitchenham and Charters who stated that the method consists of three primary stages: (1) planning the SLR, (2) conducting the research, and (3) reporting the outcomes.<sup>8</sup> The phases also comprise the following tasks: explaining the inclusion and exclusion criteria, documenting a feasible search strategy, developing the resulting study process, data extraction, and synthesis of the outcomes.

#### 2.2. ELIGIBILITY AND CRITERIA

The systematic review included articles that met the following criteria: cohort studies and randomized control trials (RCTs) evaluating pharmacological interventions for managing PONV, studies with the adult patient population (above 18 years), studies where patients underwent surgery after taking antiemetic medication in the preoperative phase, and RCTs that compare the efficacy and severe effects of single or multiple doses of antiemetic drugs. The systematic review included all the studies that have examined the effectiveness of one or more classes of antiemetic medication, including receptor antagonists, such as 5-HT<sub>3</sub>, D<sub>2</sub>, and NK<sub>1</sub>, or antihistamines, corticosteroids, and anticholinergics. Further, only full-text articles and those published in English were eligible for this study. The review omitted all abstract publications and studies older than five years. A general rule of thumb in medical and scientific research is to utilize resources that are not older than five years to avoid the problem of outdated information. Consequently, this explains why January 2020 was selected as the search date. Additionally, the exclusion criteria omitted all the studies that do not explicitly evaluate the effectiveness of antiemetic medications.

#### 2.3. INFORMATION SOURCES

As already described, the information for this study was retrieved from PubMed, Google Scholar, and Cochrane Library databases. Searching information from multiple databases was critical for optimal identification of all literature related to antiemetic drugs and their benefits in ameliorating the severe effects of PONV complications.

### 2.4. SEARCH STRATEGY

Information for use in this study was searched from PubMed, Google Scholar, and the Cochrane Database of Systematic Reviews (Ebsco) for studies published after January 2020 to avoid the problem of outdated information. The literature search combined both free words and MeSH terms, including "PONV" (such as "postoperative nausea and vomiting," "postoperative vomiting," and "postoperative emesis") and "antiemetic drugs" OR "antiemetic medication" (including "Neurokinin-1 receptor antagonists," "antihistamines," "anticholinergics," and "corticosteroids"). Manual search helped to supplement database search for all eligible articles.

#### 2.5. DATA COLLECTION PROCESS

The researcher extracted data using a predesigned standardized table. The information assessed included author and year of publication, study design, participants, surgery type, anesthesia, intervention, and outcome.

## 2.6. DATA ITEMS

The primary outcome evaluated was the incidence of PONV cases after 24 hours of postoperative surgery. Also, the study assessed various secondary outcomes, such as complete response (CR) demonstrated by numerous metrics, such as lack of vomiting and no requirement for either antiemetic or rescue medication for surgical patients. Apart from the complete response, other types of secondary outcomes assessed were signs of vomiting and nausea within the first 24 hours following a surgical operation and the requirement of rescue and antiemetic medication among the patients.

#### 2.7. RISK OF BIAS IN INDIVIDUAL STUDIES

The Cochrane Collaboration tool was critical in evaluating the quality of studies included in this research. Developed in 2008 and updated in 2011, the Cochrane Collaboration tool has been instrumental in determining the risk of bias in RCTs. According to Jørgensen et al., "The tool is based on seven domains: sequence generation and allocation concealment (both within the domain of selection bias or allocation bias), blinding of participants and personnel (performance bias), blinding of outcome assessors (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and an auxiliary domain: 'other bias.'" The bias is either judged as unclear, low, or high.

#### 2.8. SUMMARY MEASURES

A meta-analysis was conducted using a random-effects model to account for the heterogeneity between studies. The data analysis involved calculating the odds ratio (OR) at 95% confidence interval (CI). This comprehensive and stringent methodological approach was critical for better understanding the role and effectiveness of pharmacological interventions in managing PONV.

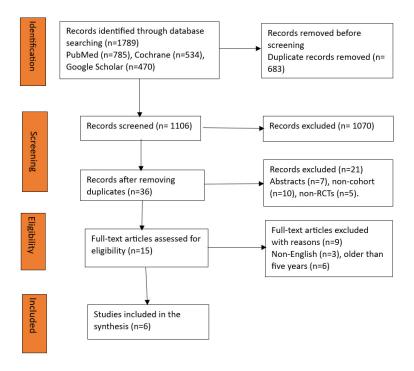


Figure 1. PRISMA diagram showing the study selection process.

#### 2.9. SYNTHESIS OF RESULTS

As already stated, odds ratios were calculated at 95% CI to examine the effectiveness of antiemetic drugs in ameliorating the adverse effects of PONV.

## 2.10. RISK OF BIAS ACROSS STUDIES

The Cochrane Collaboration tool (<a href="https://www.bmj.com/content/343/bmj.d5928">https://www.bmj.com/content/343/bmj.d5928</a>) was used to evaluate the eligibility and quality of the identified studies. The results were either unclear, low, or high among the assessed studies.

## 3.0. RESULTS

#### 3.1. STUDY SELECTION

A preliminary search of data in the three databases led to the retrieval of 1789 studies. After removing the duplicate records, only 1106 articles remained. These records were subjected to detailed screening using the inclusion and exclusion criteria, resulting in 6 studies that were included for synthesis. The PRISMA diagram (Figure 1) shows the criteria for selecting the desired articles for this study.

#### 3.2. STUDY CHARACTERISTICS

Table 1 documents the characteristics of the 6 studies included in this study. All the studies included either used the randomized-controlled trial or cohort design. The patient population underwent different surgeries, including gynecological, breast, urologic, orthopedic, rhinology, orthognathic, and elective surgery. All the patients were subjected to general anesthesia to facilitate the operations. Different antiemetic drugs were administered in the intervention

group, including dexamethasone, droperidol, ondansetron, metoclopramide, dimenhydrinate, and ramosetron.

#### 3.3. RISK OF BIAS WITHIN STUDIES

The Cochrane Collaboration tool was utilized to examine the eligibility of the six identified studies. The quality analysis is demonstrated below.

## 3.4. RESULTS OF INDIVIDUAL STUDIES

## 3.4.1. INCIDENCE OF PONV

The following table summarizes the incidence of PONV in the individual studies after applying the intervention and the placebo.

Using the random effects model to conduct a pooled analysis of the 6 studies showed that PONV incidence for the experimental group was (OR 0.37, 95% CI: 0.28:0.40, P <.05). The low odds ratio means that there is a low likelihood of PONV occurring or being severe after using an antiemetic drug.

#### 3.4.2. INCIDENCE OF VOMITING

All six studies reported the incidence of vomiting for patients undergoing surgical operations under anesthesia. However, after the use of antiemetic drugs, the studies reported a significant drop in postoperative nausea and vomiting complications. For instance, Shivanna et al. observed that a significant number of patients manifested signs and symptoms of vomiting between 0 and 6 hours after breast surgeries. This incidence was even higher in the O group, which had received a single dose of ondansetron, compared to the OD group, which received a combination of on-

**Table 1. Characteristics of the Included Studies** 

Author and year of publication	Study Design	Participants	Surgery Type	Anesthesia	Intervention	Outcome
Nowak et al. (2022) <sup>10</sup>	RCT	385 patients with moderate to high-risk PONV	Elective	General	PONV prophylaxis using dexamethasone, ondansetron, droperidol, metoclopramide, and dimenhydrinate	Antiemetic drugs effectively reduced the incidence of early and delayed PONV from 22.7- 18.3% and 29.9- 24.1% respectively. In high-risk patients, antiemetic drugs nearly halved the incidence rate of PONV from 31.2- 17.2% (p=0.030) and 34.4- 20.7% (p=0.040).
Kim et al. (2023) <sup>11</sup>	RCT	177 adult anesthetic patients undergoing different types of operations.	Orthopedic (n=80), rhinologic (n=47), urologic (n=29), others (n=18)	general	There were 2 intervention groups, R and DR, and one control group, C. Patients in group R were administered intravenous ramosetron, and intervention group DR was administered intravenous dexamethasone prior to inducing anesthesia and intravenous ramosetron after completing the surgery.	The study findings established that the PONV incidence in the first 48h after the operation was significantly lower in intervention groups R and DR than in control group C patients. Additionally, PONV incidence was consistent with rescue antiemetics medication usage patterns. Further, the number of patients needing rescue analgesics in the first 1h after the surgery was significantly lower in intervention groups R and DR than in control group C.
Shivanna et al. (2022) <sup>12</sup>	RCT	72 female patients aged between 20 and 70 years	Breast	general	Participants were grouped into two groups: ondansetron (O) and ondansetron and dexamethasone (OD). The first group, O, was administered 0.1mg/Kg of IV ondansetron, while the other group, OD, was	The study findings showed that the PONV incidence was 38.6% and 13.9% for patients in group O and OD, respectively, in the first 6h. The percentage of patients who required rescue medications was 30.6% and 8.3% for participants

Author and year of publication	Study Design	Participants	Surgery Type	Anesthesia	Intervention	Outcome
					administered 0.1 mg/Kg of IV ondansetron and 0.1 mg/Kg of dexamethasone.	in groups O and OD, respectively.
Yi et al. (2022) <sup>13</sup>	RCT	192 patients between 18 and 16 years old and belonging to ASA1-2. These patients were scheduled to undergo gynecological surgery at First Clinical Medical College of Weifang Medical College.	Gynecological day surgery	general	The patients were randomly assigned to either one of the two intervention groups droperidol (DD) or tropisetron (TT) group, or the DC control group. Before inducing anesthesia, DD received 5mg dexamethasone and 50 mg flurbiprofen axetil, and after 2 mins, 1mg of droperidol was administered. The DT group received 5mg of tropisetron, while the control group, DC, received 5mg of saline.	The study findings showed that the PONV prevalence of PACU patients was significantly lower for participants in DD (14.5%) and DT (26.7%) than for patients in the control group, DC (50%). After 24h, no significant differences could be observed for patients in the three groups, DD, DT, and DT.
Tan et al. (2023) <sup>14</sup>	Cohort study	1512 Patients subjected to major surgeries at Shuang Ho Hospital and administered with intravenous patient- controlled analgesia (IV- PCA).	Major surgery	General or neuraxial anesthesia	The patients were characterized into two groups, namely droperidol and control group. The former were administered with droperidol to IV-PCA, while the latter did not receive this treatment.	The study findings revealed that adding droperidol to IV- PCA played a fundamental role in significantly reducing the risk of PONV. The therapeutic benefits of antiemetic drugs were effective within the first 36h after surgery and considerably attenuated thereafter.
Xiao et al. (2023) <sup>15</sup>	RCT	120 patients aged between 18 and 65 were classified under ASA grade I or II.	hysteroscopy	Intravenous anesthesia	The patients were classified into three categories (n=40), namely the DC (dexamethasone plus saline) group, the DD (dexamethasone plus droperidol) group, and the DP (dexamethasone plus propofol)	The study findings showed that administering antiemetic drugs in groups DD and DP played a fundamental in reducing the severe effects of PONV for patients in PACU. No significant difference in PONV incidence

Author and year of publication	Study Design	Participants	Surgery Type	Anesthesia	Intervention	Outcome
					group. At the initiation of the surgery, group DC was administered with 2 mL saline, group DD received 1 mg of droperidol, and group DP was administered with 20mg propofol.	between the groups was observed within 24h. However, patients in groups DD and DP showed lower incidences of vomiting than those in the control group DC.

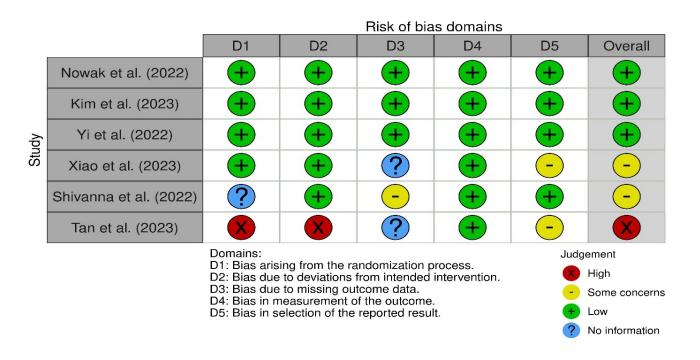


Figure 2A. Quality analysis of the six articles included in this study

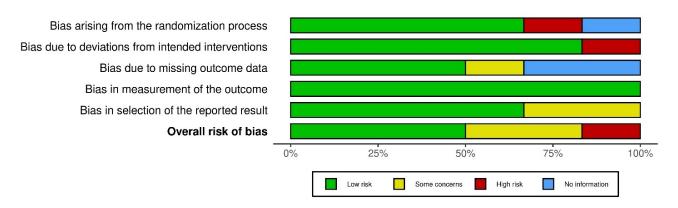


Figure 2B. Risk of bias of the six studies in graphic form.

dansetron and dexamethasone. However, none of the patients demonstrated vomiting after 12-24 hours. These

findings were similar to Kim et al., who reported that none of the patients clinically manifested vomiting within the

Table 2. Incidence of PONV

Study	Experimental	Control	PONV Incidence
Nowak et al. (2022) <sup>10</sup>	Onandenstron+dexamethasone+droperidol +metoclopramide+ dimenhydrinate	PONV prophylaxis drugs (Onandestron)	PONV incidence Early and delayed 22.7-18.3% 29.9-24.1% High-risk patients 31.2-17.2% 34.4-20.7%
Kim et al. (2023) <sup>11</sup>	R (ramosetron) DR (ramosetron +dexamethasone)	C (saline+ intravenous)	Nausea after 48h 26% (group C) 16% (group R) 9% (group DR)
Yi et al. (2022) <sup>13</sup>	DD (Dexamethasone + droperidol) DT (Dexamethasone+ tropisetron)	DC (Dexamethasone)	PONV incidence (0-24hr) 14.5% DD 26.7% DT 50% DC
Xiao et al. (2023) <sup>15</sup>	DD (Dexamethasone +droperidol DP (Dexamethasone + propofol	DC (Dexamethasone+ saline)	Nausea incidence 49% DC 12% DD 13% DP
Shivanna et al. (2022) <sup>12</sup>	OD (ondansetron +dexamethasone	O (Ondanestron)	PONV incidence 0-6h 38.9% O 13.9% OD
Tan et al. (2023) <sup>14</sup>	Droperidol +IV-PCA	IV-PCA	PONV risk after adding droperidol Adjusted Odds Risk 0.49 at 95% CI

first 48 hours after taking a dose of ramosetron or a combination of ramosetron and dexamethasone. <sup>11</sup> These findings highlight the efficacy of antiemetic medications in alleviating vomiting, particularly between 12-48 hours after the operation.

# 3.4.3. INCIDENCE OF NAUSEA

In the 2 studies that evaluated the incidence of nausea, the pooled analysis indicated that nausea was less severe in the intervention group compared to the placebo. Shivanna et al. found that none of the patients experienced nausea between 12 and 24 hours. <sup>12</sup> Likewise, Kim et al. reported that the incidence of nausea within the first 1 hour after surgery was significantly lower in the experimental groups R and DR than in the control group C. <sup>11</sup> However, no significant differences in nausea severity between the three groups could be observed between 0-48 hours.

## 3.4.4 USE OF RESCUE ANTIEMETIC DRUGS

All the studies evaluated the efficacy of either single or multiple antiemetic drugs in ameliorating the adverse signs and symptoms of PONV for patients undergoing anesthesia. All the studies reported significant inter-group differences, with the intervention groups demonstrating lower PONV incidence than the control and placebo groups. The rescue medications were more effective when combined than when used alone. For instance, Yi et al. established that PONV incidence for PACU patients was 14.5% for the group administered with dexamethasone and droperidol,

26.7% for the patients who received dexamethasone combined with tropisetron, and 50% for the control group that received dexamethasone alone. These findings were justified by Shivanna et al., who found that PONV incidence for patients administered with ondansetron alone was 38.9% and 11.1% within the first 6 and 12 hours, respectively. These incidences are slightly higher compared to the group administered with ondansetron and dexamethasone, which recorded 13.9% and 2.8% within the first 6 and 12 hours, respectively.

## **3.5.** SYNTHESIS OF RESULTS

The results of this systematic review show that the use of antiemetics for anesthetic patients after a surgical operation is critical in reducing the incidence of PONV. Tan et al.established that after administering droperidol to the experimental group, only 67 patients, translating to 12.1%, developed PONV. 14 In contrast, in the control group, 120 patients, representing 21.1%, developed PONV, demonstrating the efficacy of the rescue medications. Further, studies revealed that administering antiemetic medications alleviates severe symptoms of PONV complications, including nausea and vomiting. 11,12 The antiemetics are more effective when used in combination than when used alone. For example, Kim et al. reported that the incidence of nausea within the first 48 hours after surgery was 16% in experimental group R and 9% in intervention group DR.<sup>11</sup> It is worth noting that participants in the former experimental group were administered with ramosetron alone, while those in DR were treated with ramosetron and dexamethasone. Besides, some classes of antiemetic drugs are more effective than others. Yi et al. found that the incidence of PONV was much lower in experimental group DD (14.5%) than in intervention group DT (26.7%). Patients in DD were treated with droperidol, while those in DT received tropisetron.<sup>13</sup>

## 4.0. DISCUSSION

An extensive body of research documents that PONV prevalence is about 20-50% and that approximately 30% of patients develop post-discharge PONV. 16 Despite the widespread efforts to establish both pharmacologic and non-pharmacological interventions, PONV remains a persistent clinical problem, which increases dramatically to as high as 80% for patients who are considered at high risk.<sup>4</sup> Our study established that the use of antiemetic drugs can play a fundamental role in solving the persistent challenges associated with PONV complications. Noticeably, this study established that different types of antiemetic drugs, such as droperidol, tropisetron, dexamethasone, and ondansetron, among others, are effective in alleviating the adverse symptoms of PONV. Notably, these drugs are more efficient when utilized in combination with one another than when used alone. For example, combining ramosetron with dexamethasone increases their efficacy than when ramosetron is used alone.<sup>11</sup> Furthermore, some types of antiemetics are more effective than others. Yi et al. reported that patients treated with droperidol show better outcomes than those administered with tropisetron. <sup>13</sup> Therefore, health-care professionals must choose more effective rescue medications, especially in cases where patients demonstrate severe PONV symptoms.

Our study had numerous limitations. First, it included patients subjected to different anesthesia and surgical operations. Second, the control group included patients given either saline or antiemetic medications that functioned via different mechanisms. Third, using studies done in English and published in the last five years posed a significant limitation since it excluded literature from studies available in other languages and those a bit older that might contain rich and useful information.

# 5.0. CONCLUSION

Even though antiemetic drugs have been widely accepted in treating PONV, their efficiency differs due to numerous factors, emphasizing the need for this systematic review to guide clinical decisions and enhance patient outcomes. This study revealed that all antiemetic drugs are effective in reducing the adverse clinical signs and symptoms of PONV. However, their efficacy differs from one rescue medication to another. These findings provide supportive and practical evidence for informing future clinical treatment guidelines for patients with postoperative nausea and vomiting after undergoing surgeries under anesthesia.

Submitted: June 08, 2024 EDT, Accepted: June 18, 2024 EDT



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