

POSTOPERATIVE NAUSEA AND VOMITING: PREVENTION AND TREATMENT

Objectives

Following this presentation the participant should:

1. Appreciate the options available for both prevention and treatment,
2. Understand the difference between efficacy and outcome,
3. Recognize the limitations of routine antiemetic prophylaxis, and
4. Be familiar with a multimodal management strategy.

Introduction

Postoperative nausea and vomiting (frequently abbreviated PONV) has been characterized as the “big little problem.”¹ Historically it has been an all too common complication for both inpatients and outpatients undergoing virtually all types of surgical procedures, regardless of the anesthetic regimen used. PONV encompasses a triad of signs and symptoms. Nausea is typically described as a subjectively unpleasant sensation associated with the awareness of the urge to vomit, while vomiting is the actual physical phenomenon of the forceful expulsion of gastric contents from the mouth. Retching is physiologically similar to vomiting and is defined as the labored spasmodic rhythmic contractions of the respiratory muscles without expulsion of gastric contents. PONV thus encompasses not only physical signs (i.e., retching and vomiting) but also the unpleasant subjective feeling (nausea) experienced by the patient. A given episode of PONV can manifest any or all of these signs and symptoms and can last from minutes to hours or even days.

Risk Factors

The epidemiology of PONV is well described in the literature. Historically, a variety of independent factors have been said to be associated with the occurrence of PONV. These can be divided into non-anesthetic, anesthetic, and postoperative-related factors. Typically, younger age, female gender, large body habitus, history of motion sickness or prior history of PONV, anxiety, concomitant disease, and longer duration of surgery have all been said to be contributors to an increased incidence of PONV. Females have been noted to have an increased incidence of PONV, even after correction for surgical procedure. In addition to the gender bias for development of PONV, the day of the female menstrual cycle has also been implicated as a risk factor for the development of PONV. More recently, smoking has been implicated as well. Patients who have a history of smoking are reported to be at a decreased risk for PONV.

Site of operation or type of surgery has also been well documented as an independent risk factor for the development of PONV. Typically, head and neck procedures involving the oropharynx, auditory system, or eyes, and intra-abdominal procedures, particularly laparoscopy, have all been shown to have increased incidence of PONV. In addition, anxiety, obesity, concomitant disease, and gastroparesis have all been reported to increase the incidence of PONV. However, many of these associations are not well-established in recent literature, despite the frequent reference to these factors as risk factors for PONV in review articles.²

Various factors related to the administration of an anesthetic have also been implicated in PONV. These factors include the type of preanesthetic medication used, gastric distention occurring during the course of the anesthetic and/or surgery, gastric suctioning, and the specific

anesthetic technique. Typically, the administration of opioids as part of a preanesthetic regimen, or during the course of an anesthetic, has been shown to increase the incidence of PONV. However, this association is not completely clear cut, as will be discussed below. General anesthesia carries a higher risk of PONV than does regional anesthesia, major conduction anesthesia (subarachnoid or epidural block), or monitored anesthesia care. Neither of the latter, however, has resulted in a zero incidence of PONV. Various factors associated with the administration of general anesthesia have been implicated as causative factors for PONV. Perhaps the most controversial of these is the independent risk associated with the administration of nitrous oxide.³ No major differences have been noted in the incidence of PONV between isoflurane or enflurane anesthesia. In most, though not all cases, an opioid-based technique has resulted in a higher incidence of PONV. This may or may not be a function of the specific opioid (i.e., fentanyl, sufentanil, or alfentanil) which is used. Data suggest that the incidence and severity of PONV following sevoflurane and desflurane anesthetics may be similar to PONV after isoflurane anesthesia. On the other hand, the risks of PONV associated with a propofol-based anesthetic appear to be substantially lower than that for anesthesia maintained with potent inhalation agents.⁴

Various postoperative factors have also been implicated in the development of PONV. These include pain, dizziness, ambulation, oral intake, and the use of opioid analgesics. In a study by Andersen,⁵ paradoxically, the administration of opioids in PACU with the subsequent relief of pain actually resulted in a decrease in the incidence of nausea. In patients who complained of both pain and nausea, 68.5% experienced relief of their nausea when pain was relieved by administration of an opioid analgesic.

Recently several authors have reexamined the issue of risk factors associated with the development of PONV. Gender, age, smoking history, history of PONV or motion sickness, and duration of anesthesia have been suggested as risk factors for PONV. Several authors have all independently identified these factors and have proposed risk scoring systems based on logistic regression modeling which then assigns weights to the various factors.⁶⁻⁸ Independent evaluation of these risk scoring systems has confirmed their validity.⁹ Attempts have also been made to simplify the risk scoring systems to eliminate the need for complicated formulas. Four predictors were considered: female gender, history of motion sickness or PONV, nonsmoking, and use of postoperative opioids. If none, one, two, three, or four of these risk factors were present, the incidences of PONV were 10%, 23%, 39%, 61%, and 79% respectively.¹⁰

Pharmacologic Approaches to Management

The introduction of serotonin antagonists (specifically the 5-HT₃ subgroup) in the early 1990s offered considerable promise for the management of PONV.^{11,12} At last count, 5 different serotonin antagonists have been identified as having therapeutic efficacy in managing PONV. Of these, two (ondansetron and dolasetron) are currently approved for this indication in the United States. Prophylactic administration has been shown to decrease the incidence of PONV in various patient populations. Numerous studies have attempted to define both the optimal dose and optimal timing of administration when these medications are administered prophylactically. For ondansetron, the optimal dose for prophylaxis seems to be 4 mg administered intravenously¹³ at the end of surgery, prior to emergence.^{14,15} When used for treatment, 1 mg of ondansetron administered intravenously is as effective as higher doses.^{12,16} The optimal dose of dolasetron appears to be 12.5 mg for both prevention and treatment; however, timing of administration for prophylaxis appears to be less important than for ondansetron. Comparisons of ondansetron and

dolasetron for PONV prophylaxis suggest that there are no clinically or statistically significant differences between these medications.

Granisetron, tropisetron, ramosetron, and palonosetron have also been evaluated for the management (either prevention or treatment) of PONV. In all cases these medications have been shown to be effective (i.e., superior to placebo in randomized prospective clinical trials); however, only granisetron is currently approved (for chemotherapy-induced emesis) in the United States. The average wholesale price (AWP) of granisetron is approximately \$175 per dose. Even with purchasing agreements the acquisition cost may still exceed \$100 per dose, effectively precluding its use in the management of PONV. None of the other 5-HT₃ antagonists mentioned are currently available in the United States.

Other classes of medications are also available for prevention and treatment of PONV. These include butyrophenones (e.g., droperidol), benzamides (e.g., metoclopramide), antihistamines (e.g., promethazine, dimenhydrinate), steroids (e.g., dexamethasone), phenothiazines (e.g., promethazine, prochlorperazine), and anticholinergics (e.g., scopolamine). All are available as generic formulations and are considerably less expensive than the 5-HT₃ antagonists; however, various side effects including sedation, dysphoria, and extrapyramidal reactions have been a concern for clinicians, particularly when treating outpatients. Nevertheless, many of these generic medications (e.g., droperidol,¹⁷ dexamethasone¹⁸) are effective when administered prophylactically.

Numerous trials have been undertaken to compare the efficacy of 5-HT₃ antagonists with that of older generic medications. Most commonly studies have compared the efficacy of ondansetron with either droperidol or metoclopramide. A large (2061 patients) multicenter (50 institutions) study of ondansetron vs. droperidol for preventing PONV in high-risk patients found that droperidol in doses of either 0.625mg or 1.25 mg compared favorably with ondansetron 4 mg in outpatients.¹⁹ A recent meta-analysis has suggested that the 5-HT₃ antagonists are more effective than droperidol in preventing PONV;²⁰ however, the number needed to be treated (NNT) was 14, suggesting at best a very small beneficial effect. The efficacy of metoclopramide in preventing PONV has been questioned.^{21,22} Metoclopramide in the doses typically employed for PONV prophylaxis appears to be inadequate for a clinically significant effect and cannot be recommended for this indication.

Recently, it has been shown that combinations of antiemetics administered prophylactically appear to be more effective than either antiemetic alone. For instance the combination of ondansetron and droperidol is more effective than either of the two medications alone.²³ The same is true for the combination of ondansetron and dexamethasone.¹⁸

As noted above, the use of propofol for maintenance of anesthesia appears to result in lower incidences of PONV than are observed when anesthesia is maintained with potent inhalation anesthetics. This has led to the speculation that propofol may in fact not only be an anesthetic with a low potential for nausea and vomiting, but that it may also possess specific antiemetic properties. Numerous studies (see Table 1) have attempted to resolve this issue. As shown in Table 1 the results have been mixed. While it appears that relatively low doses of propofol may be sufficient to control symptoms in PACU,^{24,25} it may be necessary to achieve higher plasma levels of propofol intraoperatively in order to prevent PONV from occurring during PACU stay.

Adjuvants to Management

A variety of non-pharmacologic approaches to management of PONV have been investigated. These include stimulation of the Nei-Guan P6 acupoint, use of supplemental

oxygen (i.e., $\text{FiO}_2 > .30$) perioperatively, and aggressive intravenous rehydration. Stimulation of the P6 acupoint has been carried out using a variety of techniques including acupuncture, electroacupuncture, transcutaneous acupoint electrical stimulation (TAES), and acupressure. These techniques have been shown to be effective in treating both motion sickness and pregnancy-induced vomiting. Recently a multicenter, randomized, double-blinded, placebo, and sham-controlled study of TAES using the ReliefBand® device (now commercially available) demonstrated a significant decrease in the incidence of moderate-to-severe nausea as determined by the Functional Living Index-Emesis score for up to 9 hours following surgery.²⁶ Use of the device, however, did not reduce the incidence of vomiting.

Administration of supplemental oxygen (i.e., $\text{FiO}_2 = .8$, balance nitrogen) intraoperatively and for the first 2 hours postoperatively decreased the incidence of PONV (i.e., vomiting and any complaint of nausea) from 30% to 17% ($p = 0.027$) in patients undergoing colon resection.²⁷ The benefit of supplemental oxygen appears to remain intact if the higher concentration (i.e., $\text{FiO}_2 = .8$) is administered only during the intraoperative portion of the patients care. In fact 80% intraoperative oxygen reduced the incidence of PONV over the first 24 hours by half (44% vs. 22%) compared to 30% oxygen in patients undergoing gynecologic laparoscopy. This reduction was greater than that observed in patients receiving ondansetron 8 mg IV as prophylaxis.²⁸

Aggressive intravenous rehydration also appears to decrease the incidence of a number of postoperative symptoms. Patients receiving 20 mL/kg of IV fluid had a decreased incidence of thirst, drowsiness, and dizziness compared to those patients receiving 2 mL/kg. Vomiting was also decreased, though statistical significance was not achieved until postoperative day 1.²⁹

Efficacy versus Outcome

Despite the undeniable efficacy of currently available approaches to management of PONV, little evidence yet exists to show that “objective” measures of outcome are affected by current methods of management of PONV. It has been proposed that end points such as duration of PACU stay, incidence of unplanned admissions, and patient satisfaction³⁰ should be evaluated in addition to simple measures of efficacy such as frequency of vomiting or severity of nausea. An even more basic approach would be to attempt to define the effects of management of PONV on the basic measures of outcome, which would include mortality, morbidity, cost, and patient satisfaction.

Modern anesthesia has reached unparalleled levels of safety. It has been estimated that the incidence of death attributable solely to anesthesia is as low as 1:250,000 anesthetics.³¹ Given this extremely low mortality, it seems very unlikely that further reductions by alterations in management of PONV can occur, even if PONV could be eliminated entirely. Changes in morbidity seem a more likely area for improvement. Lists of complications which have been attributed to PONV include dehydration, electrolyte imbalance, tension on sutures and potential evisceration, venous hypertension and bleeding, aspiration, and delay in discharge (particularly for outpatient surgery). It is, however, difficult to quantify the frequency of these complications occurring directly as a result of PONV. It is easier to estimate the incidence of unanticipated admission following outpatient surgery and the factors that contributed to that admission. In a classic study by Gold,³² the three most common causes for admission following outpatient surgery, in a group of 9,616 adult patients who underwent ambulatory surgery between 1984 and 1986, were listed as pain, bleeding, and intractable vomiting. Each of these three groups represented approximately 20% of the total number of patients who were admitted unexpectedly. However, of the 9,616 patients who were studied, only 100 were actually admitted.

Consequently, the risk of admission related solely to intractable vomiting was less than 0.2%. While the incidence of PONV in certain patient subgroups undergoing outpatient surgery can be as high as 50-90%, the number of patients who actually have to be admitted secondary to this complication may be extraordinarily low.

In the current era of expanding managed health care, establishing the true cost associated with PONV is more important than ever. While a number of studies have attempted to quantify the economic impact of PONV,³³⁻³⁵ the ability to demonstrate significant cost savings is still lacking. Unwarranted economic assumptions are often used as justification for particular therapeutic modalities or approaches to management. It is apparent, however, that attempts to lower cost of care by decreasing PACU stay are unlikely to be successful. Even the complete elimination of PONV will not change PACU staffing needs.³⁶ If staffing levels cannot be decreased, real savings in direct costs are not likely to be realized. Other studies have attempted to provide economic justification by including the “cost” associated with unanticipated admissions due to PONV, assessed as the fully allocated cost of a day of hospitalization.³⁷ The actual cost to the institution is not the “fully allocated” cost; rather, the true cost to the institution is additional incremental (or “marginal”) cost associated with that admission. While complications related to PONV and their associated costs are an important consideration, the true incidence of these complications and the associated costs are, at best, poorly demonstrated.

Regardless of the true economic consequences, PONV does play an important role in patient satisfaction. A strong preference for limiting emetic symptoms has been demonstrated in patients.³⁸ Preoperatively, patients were asked to rate by rank order and relative value 10 possible postoperative outcomes from their most undesirable to their least undesirable outcome. By both ranking and relative value methodology vomiting was considered to be the least desirable outcome. Similar findings were also found by van Wijk.³⁹ When 129 patients were interviewed preoperatively, 29.7% expressed fears regarding the occurrence of PONV. In a study of 260 patients from Wake Forest University Baptist Medical Center, 20% of patients interviewed preoperatively were concerned enough to ask spontaneously about the risk of PONV.

Prevention versus Treatment

The intuitive assumption that patients would prefer to avoid PONV seems to be confirmed by the currently available studies. What is not apparent is whether routine prophylactic administration of antiemetics confers benefit beyond that which can be achieved by early aggressive treatment of symptoms, should they occur in PACU. We recently attempted to answer this question by examining the hypothesis that timely symptomatic treatment of PONV will result in outcomes (patient satisfaction, time to discharge, rate of unanticipated admission, and time to return to normal daily activity) that are equivalent to those seen with routine administration of a monotherapy prophylactic antiemetic.⁴⁰

A total of 575 patients were studied. Patients were stratified to 8 subgroups (See Table 2) based on the presence or absence of risk factors (gender, prior history of PONV or motion sickness, and emetogenic or non-emetogenic surgical procedure) for developing PONV. The frequencies of treatment needed for nausea and/or vomiting following surgery were determined for patients receiving ondansetron or placebo prophylaxis (Table 2). The incidence of symptomatic PONV ranged from 16% to 57% in those patients receiving placebo prophylaxis, and from 0% to 45% in those patients receiving ondansetron prophylaxis.

As would be expected, overall more patients who received prophylaxis required no treatment for symptomatic PONV (71.6%) than did those who received placebo (61.7%) ($p=0.012$). Of the

patients who required symptomatic treatment in PACU, there was no difference ($p=0.633$) in the need for treatment for nausea; however, the need for treatment for vomiting was approximately 2.5 times greater in those receiving placebo vs. those receiving ondansetron ($p=0.001$). There was no difference in nausea scores at time of discharge.

Comparisons of prophylaxis vs. treatment were accomplished by combining, within each of the two prophylaxis groups (ondansetron or placebo), those patients who required no PACU treatment for PONV with those who received ondansetron treatment. There was no difference in discharge times either to home or to Day Hospital (see Table 3). Confidence limits of the difference in times to discharge between active prophylaxis and placebo prophylaxis showed that improvement could be no greater than 12 minutes for outpatients and 5 minutes for patients admitted to Day Hospital with 97.5% certainty. There was also no difference in the percentage of patients admitted to Day Hospital. In addition, no patients were admitted to Day Hospital because of intractable PONV.

Patients who received prophylaxis did have a higher satisfaction score (97%) with management of PONV than those receiving placebo (93%); however, this difference was within the limit set *a priori* (i.e., 10%) as representing no clinically significant difference. The confidence limits of the differences in these satisfaction scores show that the improvement in satisfaction with control of PONV in the active prophylaxis (ondansetron) group can be no greater than 8.3% with 97.5% certainty. There was also no difference in 5-day satisfaction with the entire outpatient surgical experience between patients receiving prophylaxis vs. placebo. The confidence limits of the difference in patients reporting complete satisfaction with their outpatient surgical experience showed the difference to be no more than 9.8% with 97.5% certainty. Patient satisfaction with management of PONV was higher in subgroup E (the highest risk group) when prophylaxis was administered (100% *versus* 90%); however, this difference would not have been statistically significant had there been correction for multiple comparisons (See Table 4). Nevertheless, this difference does exceed the limits defined *a priori* as clinically equivalent. There was no difference between active prophylaxis and placebo in the times required to return to normal activity as assessed by the 24-hr and 5-day questionnaire either by individual indices or by survival analysis of all indices. This was true for the study population as well as individual groups.

While PONV may be viewed as highly unpleasant, these data indicate that there is little difference in outcomes when routine monotherapy prophylactic antiemetics are administered vs. simply treating PONV (promptly) should symptoms occur. Any differences which might occur are likely to be present in only those patients at highest risk for PONV.

Multimodal Management

Despite the apparent multifactorial nature of PONV, most attempts at limiting postoperative symptomatology have typically focused on a single contributing factor (e.g., elimination of nitrous oxide from the anesthetics regimen), a single modification in the anesthetic regimen (e.g., propofol vs. potent inhalation anesthesia), or the addition of a prophylactic antiemetic to a standardized management plan (e.g., ondansetron vs. placebo for the prevention of PONV). While this approach conforms nicely to the typical model of the scientific method, it fails to take into account the complex nature of the physiology involved in the phenomena of PONV. While a series of studies performed by the same investigator (or the same sites in a multicenter trial) could gradually define, in a step-wise fashion, the “optimal” management technique, this approach has not yet been undertaken perhaps because of the difficulty involved. Thousands of

patients would need to be studied over many years in order to define the “best” strategy for limiting or eliminating PONV. As an alternative, we have recently defined a multimodal algorithm for the management of PONV.⁴¹ The details of the original protocol are shown in Table 5A. The goal was to examine whether it would be possible to completely eliminate postoperative vomiting in the immediate (i.e., PACU) postoperative period. Female patients undergoing outpatient laparoscopy under general anesthesia were chosen for study because of the documented high incidence of PONV in this population. The algorithm was formulated to target as many factors related to PONV as possible. The multimodal approach was compared to conventional monotherapy prophylaxis (ondansetron 4 mg) and placebo. The incidence of vomiting in PACU prior to discharge was 0% compared to 7% of those receiving ondansetron and 22% of those receiving placebo. The multimodal management group also had a complete response rate of 98% compared to 76% in the ondansetron ($p<0.001$) and 59% in the placebo ($p<0.001$) groups. While this study does not define which elements of the algorithm are essential, it does seem to indicate that a zero incidence of PONV is a potentially achievable goal with currently available therapies even in a high-risk patient population.

While this particular protocol was nearly 100% effect in eliminating symptoms at least in the early postoperative period, it does suffer from being complex and not appropriate for all patients or all types of surgery. We have subsequently developed a simplified protocol (see Table 5B) which retains some of the elements of the original protocol while at the same time making use of a more standardized anesthetic technique. Our experience to date with this simplified protocol suggests that it is as effective as the original algorithm.

Post-discharge Nausea and Vomiting

PONV is not confined to the time patients spend in PACU. Symptoms may persist after inpatients are discharged to hospital rooms and after outpatients are discharged to home. Previously, little emphasis has been placed on control of post-discharge PONV. While it has been more common in recent years for studies to quantify post-discharge symptoms, there have been no studies which have specifically examined strategies to reduce PONV after patients have returned home. Despite the fact that analgesics are routinely prescribed for postoperative pain relief, little attention has been given to controlling post-discharge PONV. Measures taken to prevent or treat PONV pre-discharge may have little carryover effect. For instance, while both ondansetron and droperidol have been shown to be effective in preventing pre-discharge vomiting in children undergoing strabismus surgery, the incidence of post-discharge vomiting was unchanged when compared to those patients receiving placebo prophylaxis.⁴² When multimodal management is used in high-risk patients, pre-discharge PONV can be virtually eliminated; nevertheless, 12% of patients experienced vomiting after discharge to home.⁴¹

Two recent studies have suggested that measures can be undertaken to limit the severity of post-discharge PONV. Post-discharge administration of ondansetron may be useful in controlling symptoms in females undergoing outpatient laparoscopy.⁴³ In addition to 4 mg of ondansetron administered at induction, patients were randomized to receive an additional dose of ondansetron in the form of an 8 mg orally disintegrating tablet (ODT) or placebo 12 hours after surgery. The patients receiving the ODT experienced a marked reduction in post-discharge vomiting compared to those receiving placebo (3% vs. 23%, $p=0.02$). Similarly, in children undergoing outpatient strabismus surgery, administration of an additional dose of ondansetron immediately prior to discharge significantly delayed the time to first emetic episode (13.8 ± 3.0 vs. 5.9 ± 1.7 hrs; mean \pm SEM).⁴⁴ These studies suggest that measures can be undertaken to limit PONV once

patients have returned home following outpatient surgery. Further studies will be necessary to define optimal management strategies.

Conclusions

A variety of anesthetic, non-anesthetic, and postoperative factors have been identified that can contribute to PONV. Some of these factors can be controlled, many cannot. In circumstances in which the risk factors for PONV cannot be independently controlled, a variety of prophylactic and therapeutic interventions exist. New drugs as well as new approaches to management have resulted in marked improvements in efficacy for both prevention and treatment. While a variety of potential complications have been attributed to PONV, the exact incidence of most of these complications is unknown. The incidence of unanticipated admission following day surgery solely because of PONV remains extremely low. The actual costs associated with the purported complications of PONV or the additional costs incurred because of admission to hospital secondary to PONV remain extremely difficult to quantify. Clearly, large epidemiologic (preferably multicenter) studies are needed to answer these very important questions. Nevertheless, PONV remains an extremely important concern for patients undergoing surgery if for no other reason than the highly unpleasant subjective sensation of nausea and the physical act of vomiting. This is particularly true for patients undergoing ambulatory surgery. Considerable advances have been made in the management of PONV over the past ten years. PONV is clearly multifactorial. Multimodal management has made the goal of zero PONV a reality at least for the immediate postoperative period. There can now be a realistic expectation on the part of even high-risk patients that they can expect to be symptom-free following anesthesia and surgery. Still, it is not apparent that prophylactic administration of antiemetics confers any benefit on outcome compared to rapid symptomatic treatment of symptoms should they occur in PACU.

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Table 1. Antiemetic Effect of Propofol

Investigations	Randomized	Double-Blind	Placebo-Controlled	Effective
Chemotherapy Induced Emesis				
Scher 1992	no	no	no	yes
Borgeat 1993	no	no	no	yes
Borgeat 1994	no	no	no	yes
Postoperative Nausea and Vomiting				
Campbell 1991	yes	yes	yes	no
Borgeat 1992	yes	yes	yes	yes
Ewalenko 1996	yes	yes	yes	yes
Montgomery 1996	yes	yes	yes	no
Scuderi 1996	yes	yes	yes	no
Gan 1997	no	no	no	yes
Gan 1999	yes	yes	yes	yes

Table 2. Patient Stratification and Need for Postoperative Treatment by Risk Factors for PONV

Subgroup	RISK FACTORS			PACU TREATMENT REQUIRED BY GROUP	
	Gender	Prior History	Emetogenic Procedure*	Ondansetron	Placebo
A	Male	Yes	Yes	0%	50%
B	Male	Yes	No	25%	38%
C	Male	No	Yes	7%	25%
D	Male	No	No	16%	16%
E	Female	Yes	Yes	38%	57%
F	Female	Yes	No	45%	53%
G	Female	No	Yes	29%	31%
H	Female	No	No	14%	17%

*Emetogenic procedures - laparoscopy, strabismus surgery, middle ear surgery, herniography, tonsillectomy, adenoidectomy, uvulopalatopharyngoplasty

Table 3. Outcomes by Prophylaxis Versus Treatment - All Patients

	ONDANSETRON	PLACEBO	P-VALUE
Number of Patients	245	235	--
Time to Discharge:			
Day Hospital*	59 (55,64)	58 (53,63)	0.7510 ^{3‡}
Home*	87 (82,92)	92 (86,98)	0.2311 ^{3§}
Day Hospital/Outpatient	90/155	85/150	--
Satisfaction with Control of PONV			
Y/N (%)	230/7 (97.0%)	212/16 (93.0%)	0.043 ^{2‡}
Score (10th, 25th, median)	8,10, 10	5,9, 10	
Satisfaction Overall at 5 Days			
Score (10th, 25th, median)	7,9, 10	7,9, 10	0.7640 ⁴
NORMAL DAILY ACTIVITY			
How soon after your surgery were you able to:			
take care of yourself †(95% CI)	12.7 (11,15)	14.4 (12,17)	0.2878 ³
(% unable @ 5 days)	(2.7)	(3.1)	0.760 ²
take care of others †(95% CI)	34.5 (29,41)	36.7 (30,45)	0.6523 ³
(% unable @ 5 days)	(26.5)	(20.6)	0.260 ²
prepare meals †(95% CI)	31.2 (27,37)	35.7 (30,42)	0.2533 ³
(% unable @ 5 days)	(13.5)	(16.6)	0.397 ²
eat meals †(95% CI)	4.0 (4,5)	4.8 (4,6)	0.0668 ³
(% unable @ 5 days)	(0.4)	(0.4)	1.00 ¹
run errands †(95% CI)	51.9 (46,58)	51.0 (45,58)	0.8302 ³
(% unable @ 5 days)	(23.6)	(26.1)	0.559 ²
do household duties †(95% CI)	46.4 (41,52)	46.6 (40,54)	0.9558 ³
(% unable @ 5 days)	(20.8)	(23.3)	0.548 ²

* geo mean of time in min; † geo mean of time in hours

‡ 95% Confidence Intervals (ondansetron-placebo) diff=3.5 (0.3, 8.7)

§ 95% Confidence Intervals (ondansetron-placebo) diff=1.0 (-7.7, 9.8)

¹Fisher's Exact

²Chi-squared

³t-Test

⁴Wilcoxon Rank Sum

Table 4 . Outcomes by Prophylaxis Versus Treatment - Group E

	Ondansetron	Placebo	p-value	NNT
Number of Patients	47	42	--	
Satisfaction PONV: yes/no (%)	47/0 (100)	37/42 (90)	0.04	10
Satisfaction Overall: (11 pt scale)*	7,9, 10	8,9, 10	0.73	
Time to Discharge (95% CI) min	99 (85,114)	117 (98, 139)	0.13	

* 10th, 25th, **median**

Table 5. Management Algorithms for Prevention of PONV

A. Original Protocol	B. Simplified Protocol
<p>I. <u>PREOPERATIVE</u></p>	<p>I. <u>INDUCTION</u></p>
<p>A. Anxiolysis - 10-30 mcg/kg midazolam B. Fluid - 10 ml/kg minimum</p>	<p>A. PreO₂ B. Propofol 2 - 4 mg/kg C. Opioid prn D. Neuromuscular blockade prn C. Droperidol 10 mcg/kg D. Decadron 8 mg</p>
<p>II. <u>INDUCTION</u></p>	<p>II. <u>MAINTENANCE</u></p>
<p>A. PreO₂ B. Droperidol 10 mcg/kg C. Decadron 8 mg D. Propofol - 2 mg/kg + 200 mcg/kg/min E. Remifentanyl - 1 mcg/kg + 1 mcg/kg/min F. Intubate 90-120 seconds G. Gastric decompression</p>	<p>A. Propofol 50 mcg/kg/min B. Potent inhalation anesthetic of choice C. Nitrous oxide prn E. NMB reversal prn</p>
<p>III. <u>MAINTENANCE</u></p>	<p>III. <u>EMERGENCE</u></p>
<p>A. Propofol 200 mcg/kg/min × 5 min, then 150 mcg/kg/min × 5 min, then 100 mcg/kg/min × 5 min, then 75 mcg/kg/min × until Discontinue 10 minutes prior to end of surgery</p>	<p>A. Ondansetron 1 mg IV B. Suction oropharynx C. Extubate when awake</p>
<p>B. Remifentanyl 1 mcg/kg/min until intubated, then 0.5 mcg/kg/min until trocar, then 0.25 mcg/kg/min titrated to effect or BIS Off 2-3 minutes prior to end of surgery</p>	
<p>C. Ketorolac 30 mg IV after induction</p>	
<p>D. Ondansetron 1 mg at end of surgery</p>	
<p>E. Fentanyl 25 mcg IV 10 minutes prior to end of surgery</p>	
<p>IV. <u>EMERGENCE</u></p>	
<p>A. Suction oropharynx B. Extubate when awake</p>	
<p>V. <u>PACU</u></p>	
<p>A. 25 ml/kg total IV fluids for OSC stay B. Dramamine 12.5 - 25 mg IV prn nausea</p>	

Study Questions

1. Which of the following is the most significant risk factor for the development of PONV?
 - A. Use of a potent inhalation anesthetic
 - B. Female
 - C. NPO status
 - D. Body habitus
 - E. Anxiety
2. Which of the following is least effective for preventing PONV?
 - A. Ondansetron
 - B. Droperidol
 - C. Metoclopramide
 - D. Dexamethasone
 - E. Dolasetron
3. A variety of adverse events have been said to be caused by PONV. Of the following which has actually been documented?
 - A. Dehydration
 - B. Evisceration
 - C. Electrolyte imbalance
 - D. Unanticipated admission
 - E. Increased mortality
4. When employing multimodal management for preventing PONV, which of the following is a key element?
 - A. Avoidance of nitrous oxide
 - B. Aggressive IV hydration
 - C. Avoidance of NMB reversal
 - D. Propofol infusion
 - E. Avoidance of opioid analgesics

Answers:

1. B; 2. C; 3. D; 4. D