# BRIEF REPORTS

# Impact of Antiemetic Selection on Postoperative Nausea and Vomiting and Patient Satisfaction

Theodore Darkow, Pharm.D., Mary Lea Gora-Harper, Pharm.D., Daniel T. Goulson, M.D., and Kenneth E. Record, Pharm.D.

- **Study Objective.** To determine the impact of antiemetic selection on postoperative nausea and vomiting (PONV) and patient satisfaction after ambulatory surgery.
- Design. Prospective, observational study.
- Setting. Ambulatory surgery center in an academic medical center.
- **Patients.** Five hundred fifty-four consecutive patients undergoing ambulatory surgical procedures of any kind.
- **Intervention.** Data on antiemetic utilization, occurrence of PONV, and patient satisfaction were collected perioperatively. Multiple regression analyses for antiemetic choice were performed.
- **Measurements and Main Results.** Prophylactic antiemetic therapy was administered to 292 (52.7%) patients, most often with droperidol (200 patients), metoclopramide (134), or dexamethasone (55). Forty-one (7.4%) patients had an episode of emesis in the postanesthesia care unit. Choice of antiemetic was not a significant predictor of PONV. Patient satisfaction for all patients was 9.5 on a 10-point scale, with no agent more or less successful than any other.
- **Conclusion.** As choice of antiemetic drug given for prophylaxis had little impact on clinical outcome or patient satisfaction, traditional agents should form the core of antiemetics used for PONV prophylaxis in ambulatory surgery patients.

#### (Pharmacotherapy 2001;21(5):540–548)

Advances in surgical methods have allowed many procedures to be performed on an ambulatory basis, improving patient outcomes and decreasing associated costs.<sup>1</sup> Unfortunately, postoperative nausea and vomiting (PONV) continues to have negative clinical and economic consequences.<sup>1-4</sup> Published rates of PONV in ambulatory surgery patients vary widely, ranging from 5–45%.<sup>2, 3, 5</sup> Occurrence of PONV after ambulatory surgery can lead to increased postoperative pain, electrolyte loss, and longer recovery time in the postanesthesia care unit (PACU). Severe cases of PONV may even lead to unanticipated hospitalization and inability to return to work.<sup>2</sup> Negative effects from PONV are not limited to the patient; the increased resources and time needed to treat a patient with PONV can have a profound economic impact on the surgical unit.<sup>3, 4</sup> Annual cost of PONV to a typical ambulatory surgical unit was estimated to be as high as \$1.5 million.<sup>3</sup>

Although much attention has been given to PONV in recent years, the physiology and causes of PONV remain poorly understood.<sup>2, 6</sup> Current

From the College of Pharmacy, University of Kentucky, (Drs. Darkow, Gora-Harper, and Record); and the Department of Anesthesiology, University of Kentucky Chandler Medical Center (Dr. Goulson), Lexington, Kentucky.

Address reprint requests to Mary Lea Gora-Harper, Pharm.D., Drug Information Center (C-118), University of Kentucky Hospital, 800 Rose Street, Lexington, KY 40536-0293.

literature suggests that the incidence of PONV is affected by surgical procedure, patient-specific factors, anesthesia-related factors, and postoperative factors.<sup>2, 5, 7-14</sup> Although investigations of PONV thoroughly examined risk factors relating to patient and surgery characteristics, how the choice of preoperative antiemetic drugs relates to PONV and other postsurgical outcomes has not been investigated in general surgery populations. Randomized trials of antiemetic effectiveness compared drugs in specific populations, but these results cannot be applied easily to the entire surgical population. Some studies even suggested that antiemetic prophylaxis offers no advantage over symptomatic treatment.<sup>15-17</sup> A better understanding of the effects of preoperative drug use on PONV is needed to improve postoperative outcomes and provide patients with the best possible care. Currently, there is no standard in antiemetic prophylaxis of PONV at our institution; antiemetic regimens are individually chosen by each patient's anesthesia provider.

Patient satisfaction with drugs used for PONV prophylaxis was examined in previous studies<sup>18-21</sup>; however, methodologic concerns and study limitations prevent extrapolation of those findings to a standard ambulatory surgery population. It was suggested that many factors, such as patient expectations and adverse effects from antiemetic drugs, influence patient satisfaction.<sup>19, 20</sup> Therefore, indirect measures of satisfaction, such as incidence of PONV, offer little insight into the patient's perception of success.

We conducted a prospective, observational investigation from the institution's perspective to determine the impact of antiemetic selection on postoperative emesis, recovery time in the PACU, and patient satisfaction in ambulatory surgery patients at the Kentucky Surgery Center. Secondary outcomes for this investigation included postoperative nausea, delayed discharge secondary to PONV or drug side effects, and unanticipated hospitalization for management of PONV.

# Methods

The Kentucky Surgery Center is a seven-room operating room suite within the University of Kentucky Hospital, where surgeons perform about 6000 procedures/year. Most procedures are performed on ambulatory patients, although minor surgical procedures sometimes are done on inpatients. All surgical subspecialties are represented. Patients are both adults and children.

To achieve the desired sample of 500 patients, consecutive patients at the Kentucky Surgery Center undergoing surgical procedures of any kind were enrolled in the study during a 6-week period. Patients could be any age and scheduled for a procedure of any length. Data on PONV risk factors and postoperative outcomes were collected both pre- and postoperatively by using a standard data collection form developed by the investigators. Missing or unclear data were verified through retrospective examination of patients' anesthesia records and medical records. The study protocol was approved by the institutional review board of the University of Kentucky Medical Center.

During the preoperative interview, an operating room nurse or the patient's anesthesia provider determined preoperative PONV risk factors by collecting data on age, weight, gender, smoking status, history of PONV or motion sickness, and last oral intake. Each patient's operating room nurse also recorded the patient's preoperative anxiety on a 10-point scale (0 = no anxiety, 10 = severe anxiety), as other investigators suggested it was a predictor of PONV.<sup>14, 22</sup> Immediately after surgery, data on intraoperative risk factors such as type of surgery, intubation procedure, type of anesthesia, specific anesthetic agents used, duration of procedure, time under anesthesia, and perioperative drugs were recorded.

All data during the patient's recovery in the PACU were recorded by the patient's primary recovery nurse. Postoperative pain was assessed throughout the patient's stay in the PACU using a 10-point scale<sup>11, 23</sup>; the patient's worst pain while in the PACU was recorded on discharge. Level of nausea, measured by a 10-point scale (0 = nonausea, 10 = severe nausea)<sup>2,24-26</sup> and episodes of emesis were recorded at 10, 30, 60, and 120 minutes after transfer to the PACU. When PONV occurred, antiemetic drugs given for acute treatment of PONV were recorded; their effectiveness, defined by a decrease in level of nausea, was noted. Immediately after patient discharge, total time spent in the PACU was recorded and the patient's recovery nurse reported whether discharge from the unit was delayed due to PONV or drug side effects such as drowsiness and extrapyramidal side effects. Unanticipated hospitalization for intractable nausea or vomiting immediately after surgery also was noted by the recovery nurse at this time.

0 1	· /		
Characteristic	Value	SD	95% CI
Female gender (%)	51		
Mean age (yrs)	35.6	23.9	33.6 - 37.5
Mean weight (kg)	66.1	31.4	63.5 - 68.7
Obesity (%) <sup>a</sup>	23		
History of smoking (%)	23		
History of PONV (%)	16		
History of motion sickness (%)	12		
Delayed gastric emptying (%) <sup>b</sup>	23		
Preoperative anxiety <sup>c</sup>	4.7	2.6	4.4 - 4.9

Table 1. Patient Demographics (n=554)

PONV = postoperative nausea and vomiting.

<sup>a</sup>Defined as  $\geq 125\%$  ideal body weight.

<sup>b</sup>Defined as at least one of the following: gastroesophageal reflux disease, gastrointestinal obstruction, diabetes mellitus, or chronic cholecystitis.

<sup>c</sup>Based on a 10-point scale (0 = no anxiety; 10 = highest possible anxiety).

Finally, patient satisfaction at discharge with the prevention and overall control of PONV was assessed using a standard 10-point scale, with a score of 10 being the highest level of satisfaction.<sup>18</sup> Patients were defined as being highly satisfied if their satisfaction scores were 8.0 or above.

#### Data Analysis and Statistics

Data were placed into multiple regression equations to determine whether choice of pre- or postoperative antiemetic drugs had an impact on postoperative outcomes. Regressions were performed for seven response variables: incidence of postoperative emesis, incidence of postoperative nausea, time spent in the PACU, delayed discharge secondary to PONV, delayed discharge secondary to drug side effects (drowsiness or extrapyramidal side effects), unanticipated hospitalization for PONV, and patient satisfaction score. Independent variables (predictors) included in all regressions were antiemetic drugs (including dose) used for PONV prophylaxis or rescue, number of drugs given for prophylaxis, and timing of antiemetic prophylaxis (preoperative, induction, or end of surgery). A  $\chi^2$  analysis was used to compare emesis rates for specific antiemetic regimens; mean time to recovery with specific antiemetic agents was compared by Student's t test. Patient satisfaction score among specific antiemetic agents was compared by the Kruskal-Wallis test. All statistical calculations were performed using the SAS Statistical Software, version 8, for Windows 95 (SAS Institute, Cary, NC).

Table 2. Surgery and Anesthesia Characteristics

Table 2. Surgery and Anestnesia	Characteristics		
	No. of Pts with Emesis/		
Characteristic	Total No.		
Type of Surgery			
Ophthalmologic	8/160		
Orthopedic	8/108		
Ear, nose, or throat	11/106		
Plastic	3/23		
Intraabdominal	0/15		
Laparoscopic	2/15		
Gynecologic	2/13		
Major breast	2/9		
Unclassified or miscellaneous	5/105		
Endotracheal Intubation	27/255		
Duration of surgery (min)			
< 30	10/143		
30-59	8/164		
60-89	4/92		
90-119	3/59		
120–149	6/38		
150-179	5/25		
180-210	2/18		
> 210	3/13		
Anesthetic agent <sup>a</sup>			
Propofol	26/334		
Sevoflurane	13/210		
Desflurane	27/180		
Nitrous oxide	8/81		
Thiopental	5/23		
Isoflurane	1/18		
Etomidate	0/3		
Ketamine	0/3		
Methohexital	0/1		
Duration of anesthesia (min)			
< 60	3/143		
60-119	3/245		
120-179	13/105		
180-240	13/40		
> 240	9/21		
Opioid administration			
Preoperative	12/188		
Intraoperative	36/421		
Postoperative	16/198		
<sup>a</sup> Patients may have received more than one anesthetic agent.			

<sup>a</sup>Patients may have received more than one anesthetic agent.

#### Results

### Patient and Surgery Characteristics

Data were collected on 554 consecutive patients (281 females). A description of the surgical population is given in Table 1. Mean age of all patients was 35.6 years (95% confidence interval [CI] 33.6–37.5). With 155 (28%) patients under 18 years of age, there was a sizable pediatric population. Mean age of the pediatric patients was 6.1 years (95% CI 5.3–6.9); mean age of adult patients was 47.0 years (95% CI 45.2–48.8). The population included 125 (23%) obese patients, defined as weighing at least 125%

0		1 5		
	No. (%)	Timing of Ant	iemetic Prophy	ylaxis, no. (%) <sup>b</sup>
Agent <sup>a</sup>	of Patients	Preoperative	Induction	End of Procedure
Droperidol	200 (36)	27 (14)	135 (68)	29 (15)
Metoclopramide	134 (24)	50 (37)	64 (48)	17 (13)
Dexamethasone	55 (10)	c	c	c
Famotidine	51 (9)	31 (61)	17 (33)	2 (4)
Dolasetron	8 (1)	2 (25)	3 (38)	3 (38)
Hydroxyzine	6(1)	3 (50)	2 (33)	0 (0)
Ondansetron	1 (0.2)	0 (0)	0 (0)	1 (100)

Table 3. Agents Used for Antiemetic Prophylaxis

<sup>a</sup>Patients may have received more than one agent.

<sup>b</sup>Numbers may not add up to 100% due to missing values.

<sup>c</sup>Data on timing of dexamethasone prophylaxis not collected.

ideal body weight. History of PONV or motion sickness was reported by 86 (16%) and 68 (12%) of patients, respectively. Information on surgical procedures performed and other relevant surgery characteristics is shown in Table 2. The most common surgical procedures were ophthalmologic (160 patients), orthopedic (108), and ear, nose, or throat surgery (106). Endotracheal intubation was used in 255 (46%) patients, and propofol was used for induction or maintenance of anesthesia in 334 (60%) patients. The duration of surgery was less than 2 hours in 458 (83%) procedures. Mean postoperative pain score for all patients was 2.2 (95% CI 1.9–2.5).

#### **Clinical Outcomes**

Evaluation of the data found that antiemetic prophylaxis was given to 292 (52.7%) patients (Table 3.) When prophylaxis was given, the most common antiemetic agents were droperidol (200 patients), metoclopramide (134), and dexamethasone (55). While in the PACU, 41 (7.4%) patients had at least one episode of postoperative emesis. No single antiemetic drug was a significant predictor of emesis in the PACU. Number of drugs used concurrently for PONV prophylaxis was also not significant.

Twenty-one (8.0%) of the 262 patients receiving no antiemetic prophylaxis experienced at least one episode of emesis. Postoperative emesis occurred in 15 (13.2%) of 114 patients receiving only droperidol for PONV prophylaxis. Of the 200 patients receiving droperidol either alone or in combination with other antiemetics, 24 (12.0%) experienced postoperative emesis. Three (12.5%) of the 24 patients receiving dexamethasone as the only preoperative antiemetic had at least one episode of postoperative emesis; six (10.9%) of 55 patients receiving dexamethasone with or without other antiemetics experienced postoperative emesis. None of the 38 patients receiving metoclopramide alone for PONV prophylaxis experienced postoperative emesis. Of the 134 patients receiving metoclopramide either alone or as part of a multidrug prophylaxis regimen, nine (6.7%) patients experienced postoperative emesis. Differences between metoclopramide and both other agents when used alone were statistically significant (droperidol, p=0.02; dexamethasone, p=0.03). However, no difference between the agents was statistically significant when they were used in combination with other antiemetics.

As a secondary outcome, frequency of nausea in the PACU was examined. During the investigation, 124 (22.4%) patients reported experiencing feelings of nausea while in the PACU. No single antiemetic agent was a predictor of nausea in the PACU, nor was number of drugs used concurrently for PONV prophylaxis.

#### **Recovery Time**

Mean time (SD) to recovery and discharge from the PACU for all patients was 69 (31) minutes. Mean time (SD) to discharge from the PACU was over 50% longer [107 (55) min, p<0.0001] for patients with postoperative emesis. Patients who received no antiemetic prophylaxis stayed in the PACU for an average of 62 (28) minutes; mean time in the PACU for patients receiving PONV prophylaxis was 77 (32) minutes (p<0.0001). Evaluation of the regression equation for time in the PACU indicated that no individual antiemetic drug had a significant impact on time to recovery, nor did number or timing of drugs given for prophylaxis. When presence or absence of emesis was added to the regression equation, occurrence of an emetic episode was an extremely strong predictor of increased time to

recovery and delayed discharge from the PACU (p<0.0001).

Delayed discharges from the PACU secondary to either PONV or drug side effects were examined as secondary outcomes; unanticipated hospitalization for PONV was also measured as a secondary outcome. Twenty-one (51.2%) of the 41 patients with postoperative emesis were identified as having a delay in discharge secondary to PONV; intractable PONV was experienced by five patients, leading to unanticipated hospitalization. All patients hospitalized for PONV had undergone emetogenic procedures and had received antiemetic prophylaxis. Neither choice of antiemetic regimen nor timing of antiemetic prophylaxis was a predictor of delayed discharge or hospitalization for PONV.

Fifteen patients were delayed from being discharged from the PACU secondary to drug side effects, specifically drowsiness. All received at least one drug known to cause drowsiness while in the PACU; nine received two or more sedating drugs. Twelve (80%) of the fifteen patients received an opioid for postoperative pain control, nine (60%) patients received droperidol for PONV rescue, and five (33%) patients received either promethazine or hydroxyzine for PONV rescue. Evaluation of the regression equation found that postoperative administration of either an opioid (p=0.008) or droperidol (p=0.001) was a significant predictor of delayed discharge from the PACU secondary to drowsiness. Mean time (SD) to recovery in all patients receiving a postoperative opioid was higher than the mean (SD) for all patients [79 (30) vs 69 (31) min, p=0.0002]; mean time (SD) to recovery for patients receiving PONV rescue with droperidol was 101 (38) minutes (p<0.0001).

# **Patient Satisfaction**

Patient satisfaction with prevention and control of PONV was very high, overall; a high satisfaction rating ( $\geq 8.0$ ) was achieved in 93% of patients. No individual antiemetic drug was found to be better or worse (p>0.05). When presence or absence of postoperative emesis was added to the regression equation, occurrence of emesis was determined to be the strongest predictor of patient dissatisfaction (p<0.0001). This regression also showed a trend for higher patient satisfaction when droperidol was used for PONV prophylaxis (p=0.09). A third regression

Table 4. Agents Administered for PONV Rescue

	No. (%) of Pts	
Agent <sup>a</sup>	Receiving Agent	% Effectiveness
Droperidol	38 (48)	68
Metoclopramide	14 (18)	64
Promethazine	10 (13)	60
Dolasetron	9 (11)	33
Hydroxyzine	3 (4)	67
Ephedrine	3 (4)	67
Prochlorperazine	1 (1)	100
Ondansetron	1 (1)	0
Totals	79 (100)	57

<sup>a</sup>Patients may have received more than one agent.

for patient satisfaction was performed, which included postoperative use of opioids as potential predictors, as well as all antiemetic agents used for PONV rescue (Table 4). Four different antiemetics—droperidol, promethazine, prochlorperazine, and ondansetron—were associated with a statistically significant decrease in patient satisfaction when used for PONV rescue (p<0.001). Although a trend toward lower satisfaction in patients receiving postoperative opioids was seen, it was not statistically significant (p=0.09).

## Discussion

The rate of postoperative emesis seen during the investigation was comparable with other reports of PONV in ambulatory patients.<sup>2, 3, 5</sup> No agent showed greater success in relation to frequency of PONV in these patients, nor did choice of antiemetic agent have a significant impact on recovery time, hospitalization, or patient satisfaction.

Although several investigations have been conducted to determine the best antiemetic regimen for PONV prophylaxis, results are hard to compare because of small sample sizes and differences in patient selection, surgery and anesthesia type, and patient outcomes. Some suggested that antiemetic prophylaxis offers no advantage over symptomatic treatment of PONV,<sup>15-17</sup> but several meta-analyses and randomized trials showed that routine antiemetic prophylaxis, used judiciously in high-risk patients, can be a cost-effective practice.<sup>2, 27-31</sup>

All antiemetic agents were equally effective in preventing postoperative emesis. Because occurrence of postoperative emesis had the largest impact on time to recovery and discharge from the PACU, as well as on patient satisfaction, it is not surprising that no agent had better results than the others on these measures of patient recovery when evaluated by linear regression. This is in disagreement with previous studies, which suggested that comparative efficacy for the prevention of PONV can be summed up as follows: serotonin 5-HT<sub>3</sub> receptor antagonists > droperidol > metoclopramide  $\geq$  placebo.<sup>2, 32-34</sup>

Since only nine patients in this study received a 5-HT<sub>3</sub> receptor antagonist, it is difficult to draw any conclusions regarding these agents. Data from 53 trials involving 7177 ambulatory and inpatient surgery patients were combined and evaluated by meta-analysis to determine the efficacy, dose-response, and safety of ondansetron in the prevention of PONV.<sup>35</sup> Ondansetron, given prophylactically, consistently decreased the frequency of PONV. The optimum intravenous dose of ondansetron was 8 mg. Other 5-HT<sub>3</sub> receptor antagonists have had similar effects on PONV.<sup>2, 20, 21</sup>

The large numbers of patients receiving dexamethasone, droperidol, and metoclopramide for PONV prophylaxis allow for comparison by descriptive and evaluative statistics. Dexamethasone has been used successfully in the prevention of chemotherapy-induced emesis. Interest has grown recently in using this agent as prophylaxis for PONV, especially in combination with other antiemetics. Our investigation did not specifically examine the combination of dexamethasone with a 5-HT<sub>3</sub> receptor antagonist; however, all regression equations examined the number of antiemetic drugs given concurrently for prophylaxis as a predictor of success or failure. Data did not show better outcomes with multiple-drug regimens, in contrast to previous studies in the literature.<sup>36-41</sup>

A recent meta-analysis of 17 randomized, controlled trials involving 1946 ambulatory and inpatient surgery patients was performed to define the antiemetic efficacy and safety of dexamethasone in prevention of PONV.<sup>36</sup> Prophylactic dexamethasone was effective in reducing PONV without clinically relevant toxicity in otherwise healthy patients. The report also suggested that combining dexamethasone with a 5-HT<sub>3</sub> receptor antagonist offered even greater efficacy. This finding, although contrary to our investigation, is in accordance with other reports in the literature.<sup>37, 38</sup>

Because only 117 patients received prophylaxis with two or more antiemetics during our investigation, our study may not have had enough power to detect a significant difference in success rate for these patients. Also, because choice of antiemetic regimen was not controlled, this result may have been secondary to provider treatment bias. Each patient's anesthesiologist chose the antiemetic regimen based on patientspecific factors and personal preference, so patients at highest risk for PONV were more likely both to receive multiple-drug regimens and to experience PONV.

Droperidol was the antiemetic drug used most frequently in this study for PONV prophylaxis. Several trials examining the efficacy of droperidol for PONV prophylaxis were reviewed.<sup>2</sup> It was found that droperidol was effective in reducing the frequency of PONV in patients who underwent a variety of ambulatory and inpatient surgical procedures. It was concluded, however, that standard antiemetic doses of droperidol (0.625-1.25 mg) have limited efficacy in the most emetogenic surgical procedures. During our investigation, high-dose droperidol (> 1.25 mg) was administered to 19% of patients receiving a drug for PONV prophylaxis. No cases of akathisia or other extrapyramidal side effects were seen; additionally, no patient's delayed discharge secondary to drowsiness could be directly linked to prophylactic use of droperidol. This is in contrast to the literature, as many authors have suggested that, while higher doses of droperidol (2.5-5 mg) may be more effective in highly emetogenic procedures, the frequency of adverse effects such as drowsiness and akathisia makes these doses unacceptable in practice.2, 42-44

Our study found metoclopramide to be an acceptable alternative for PONV prophylaxis. No patient was given more than metoclopramide 20 mg for PONV prophylaxis, yet these patients had outcomes similar to those of patients receiving other antiemetic agents. This is contrary to data from a recent meta-analysis that evaluated data from 66 randomized, placebo-controlled studies enrolling 9242 ambulatory and inpatient surgery patients.<sup>45</sup> In most of the studies evaluated, the adult dose of metoclopramide was 10-20 mg. Investigators concluded that metoclopramide in those doses had little to no clinically relevant effect on PONV and that, therefore, metoclopramide should not be used for prophylaxis until the optimum dose is established. A possible reason for this discrepancy may be that metoclopramide rarely was given as the sole antiemetic agent; 96 patients receiving prophylaxis with metoclopramide also received at least one other antiemetic drug for PONV

prophylaxis, usually droperidol.

Follow-up analysis was performed with droperidol, metoclopramide, and dexamethasone, the agents used most often during this investigation for PONV prophylaxis. Comparison of emesis rates among patients receiving these drugs found that patients receiving droperidol or dexamethasone as the sole agent for PONV prophylaxis were significantly more likely to experience postoperative emesis than were patients receiving metoclopramide alone. As stated before, this result conflicts that in the literature.<sup>45</sup> A brief evaluation of the patients receiving single-agent prophylaxis with metoclopramide shows that these patients typically underwent procedures of less than 1 hour's duration and, by history, had fewer episodes of PONV. As both of these factors have been associated with a decreased risk of PONV, the deceptively positive results for metoclopramide are more likely the result of provider treatment bias than superior efficacy. It appears that metoclopramide was used in patients whom their anesthesia providers determined to be at low risk. The lowest rate of postoperative emesis was seen in patients who received no prophylactic antiemetic. This somewhat counterintuitive result is also likely to be secondary to provider treatment bias; the patients who were identified as being at lowest risk for PONV by their anesthesia providers were given no PONV prophylaxis and, not surprisingly, did not experience postoperative emesis.

One outcome that has received little attention is patient satisfaction. The patients in this study had a very high satisfaction rate, as would be expected with the low rate of postoperative emesis. Evaluation of the linear regression for patient satisfaction found no antiemetic regimen used for prophylaxis to be superior, nor did timing of prophylaxis have a significant effect on postoperative satisfaction. The second regression in our investigation, with the inclusion of incidence of postoperative emesis as a potential predictor, showed clearly that patients experiencing any postoperative emesis had a lower satisfaction rate. This was to be expected, as patients were asked how satisfied they were with prevention and control of PONV while in the PACU. Unexpectedly, however, PONV prophylaxis with droperidol was associated with increased patient satisfaction.

This is in contrast to previous reports in the literature. One study<sup>18</sup> looked at frequency of PONV and patient satisfaction after middle ear

surgery in ambulatory and hospitalized patients when preoperative promethazine was administered alone or in combination with ondansetron. Investigators found that while the combination regimen decreased both the frequency and severity of PONV, patient satisfaction was not significantly different from promethazine alone or placebo. Patient satisfaction was not the primary outcome of the investigation; therefore, the study may not have had sufficient power to detect a difference in patient satisfaction.

A well-designed study<sup>19</sup> investigating patient outcomes after elective outpatient surgical procedures was performed to compare efficacy, safety, and patient satisfaction in adult patients receiving either ondansetron or droperidol for prophylaxis of PONV. This multicenter, placebocontrolled investigation enrolled over 2000 highrisk patients to determine whether choice between these two agents had an impact on any aspect of patient recovery. The number of patients achieving what the investigators deemed a complete response and absence of nausea was significantly higher in the droperidol group than in either the placebo or the ondansetron group. Safety of the drug, measured by frequency of adverse events, was similar among all groups. Although both the droperidol and ondansetron groups in this study had higher satisfaction ratings than the placebo group, the investigators did not find a significant difference between the droperidol and ondansetron groups, even with differing rates of PONV. This result is echoed in other studies<sup>20, 21</sup> and by our investigation, as there were no significant differences between the antiemetic agents when compared by regression or the Kruskal-Wallis test.

The final regression in this investigation was performed to examine whether patient satisfaction was influenced by use of PONV rescue drugs. Use of postoperative opioids was included in the equation as well, to ensure that patient satisfaction with PONV control only, not postoperative pain, was being measured. Also, both postoperative pain and use of postoperative opioids have been shown to be emetogenic.<sup>1, 5-14</sup> The study appeared to be successful in this regard, as use of postoperative opioids was not shown to have a significant impact on patient satisfaction. Four antiemetics were shown to be associated with a statistically significant decrease in patient satisfaction when used for PONV rescue. Other antiemetic agents showed a similar trend; however, statistical significance was not achieved with these agents secondary to the small number of patients requiring PONV rescue. This result is not surprising, as use of postoperative antiemetics is an indirect indicator for postoperative emesis, which was shown to be strongly associated with decreased patient satisfaction.

Our study has limitations. As previously stated, choice of antiemetic regimen for PONV prophylaxis was based on provider preference and patient-specific factors. Whereas this provides an accurate picture of standard practice at the Kentucky Surgery Center, it makes direct comparison of antiemetic regimens difficult. Using multivariate regression analyses allows for the simultaneous examination of several possible influences on patient outcomes. Therefore, the potential impact of provider treatment bias should be minimized.

As the Kentucky Surgery Center is our institution's ambulatory surgery unit, most of the patients enrolled in this study underwent minor surgical procedures on an outpatient basis. It is not clear from the literature whether hospitalized patients undergoing inpatient surgical procedures are at increased risk for PONV secondary to poorer physical status or other perioperative factors. For this reason, results from this investigation may not be applicable to inpatient surgery units.

Finally, as this investigation was undertaken from the institution's perspective, data on PONV and other postoperative complications were collected only while patients were in the PACU. Although information on patient recovery for 24 hours postoperatively may have been helpful in discovering differences among the antiemetic regimens, the primary focus of this investigation was to determine the impact of PONV on patients while in the PACU.

#### Summary

Postoperative nausea and vomiting are a common consequence of ambulatory surgery. The frequency of postoperative emesis in this investigation was similar to that noted in other reports in the literature involving ambulatory surgery patients. Choice of antiemetic drug given for prophylaxis had little impact on clinical outcome or patient satisfaction; overall frequency of adverse events was low with these antiemetic regimens. Although we cannot draw a conclusion about the efficacy of newer 5-HT<sub>3</sub> receptor antagonists compared with agents such

as droperidol or metoclopramide, these data show a high degree of success with these traditional agents, suggesting that they should form the core of antiemetics used for PONV prophylaxis in ambulatory surgery patients. Further research is necessary to determine whether adding 5-HT<sub>3</sub> receptor antagonists to this core offers further benefit to surgical patients.

# Acknowledgement

The authors would like to acknowledge Brenda Darkow for her assistance during data collection and database entry.

#### References

- Hunter JD, Chambers WA, Penny KI. Minor morbidity after day-case surgery. Scot Med J 1998;43:54–6.
- American Society of Health-System Pharmacists. ASHP therapeutic guidelines on the pharmacologic management of nausea and vomiting in adult and pediatric patients receiving chemotherapy or radiation therapy or undergoing surgery. Am J Health-Syst Pharm 1999;56:729–64.
- Hirsch J. Impact of postoperative nausea and vomiting in the surgical setting. Anaesthesia 1994;49(suppl):30–3.
- Cohen MM, O'Brien-Pallas LL, Copplexione C, Wall R, Porter J, Rose DK. Nursing workload associated with adverse events in the postanesthesia care unit. Anesthesiology 1999;91:1882–90.
- Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? Anesthesiology 1999;91:109–18.
- Naylor RJ, Inall FC. The physiology and pharmacology of postoperative nausea and vomiting. Anaesthesia 1994; 49(suppl):2-5.
- Kenny GNC. Risk factors for postoperative nausea and vomiting. Anaesthesia 1994;49(suppl):6–10.
- Apfel CC, Laara E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. Anesthesiology 1999;91:693–700.
- 9. Apfel CC, Greim CA, Haubitz I, et al. A risk score to predict the probability of postoperative vomiting in adults. Acta Anaesthesiol Scand 1998;42:495–501.
- 10. Apfel CC, Greim CA, Haubitz I, et al. The discriminating power of a risk score for postoperative vomiting in adults undergoing various types of surgery. Acta Anaesthesiol Scand 1998;42:502–9.
- 11. Koivuranta M, Laara E, Snare L, Alahuhta S. A survey of postoperative nausea and vomiting. Anaesthesia 1997;52:443–9.
- Toner CC, Broomhead CJ, Littlejohn IH, et al. Prediction of postoperative nausea and vomiting using a logistic regression model. Br J Anaesth 1996;76:347–51.
- 13. Cohen MM, Duncan PG, DeBoer DP, Tweed WA. The postoperative interview: assessing risk factors for nausea and vomiting. Anesth Analg 1994;78:7–16.
- Palazzo M, Evans R. Logistic regression analysis of fixed patient factors for postoperative sickness: a model for risk assessment. Br J Anaesth 1993;70:135–40.
- 15. Scuderi PE, James RL, Harris L, Mims GR. Antiemetic prophylaxis does not improve outcomes after outpatient surgery when compared to symptomatic treatment. Anesthesiology 1999;90:360–71.
- Fisher DM. Surrogate outcomes: meaningful not! Anesthesiology 1999;90:355-6.
- Fisher DM. The "big little problem" of postoperative nausea and vomiting: do we know the answer yet? Anesthesiology

1997;87:1271-3.

- Khalil S, Philbrook L, Rabb M, et al. Ondansetron/ promethazine combination or promethazine alone reduces nausea and vomiting after middle ear surgery. J Clin Anesth 1999;11:596–600.
- 19. Fortney JT, Gan TJ, Graczyk S, et al. A comparison of the efficacy, safety, and patient satisfaction of ondansetron versus droperidol as antiemetics for elective outpatient surgical procedures. Anesth Analg 1998;86:731–8.
- American Society of Anesthesiologists Task Force on Pain Management, Acute Pain Section. Practice guidelines for acute pain management in the perioperative setting. Anesthesiology 1995;82:1071–81.
- 21. Morrow GR. The assessment of nausea and vomiting: past problems, current issues, and suggestions for future research. Cancer 1984;53(suppl):2267–80.
- Olver IN, Simon RM, Aisner J. Antiemetic studies: a methodological discussion. Cancer Treat Rep 1986;70:555–63.
- Gralla RJ, Člark RA, Kris MG, Tyson LB. Methodology in antiemetic trials. Eur J Cancer 1991;27(suppl):S5–8.
- 24. Watcha MF. The cost-effective management of postoperative nausea and vomiting. Anesthesiology 2000;92:931–3.
- White PF, Watcha MF. Postoperative nausea and vomiting: prophylaxis versus treatment. Anesth Analg 1999;89:1337–9.
- Hill RP, Lubarsky DA, Phillips-Bute B, et al. Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. Anesthesiology 2000;92:958–67.
- 27. Frighetto L, Loewen PS, Dolman J, Marra CA. Costeffectiveness of prophylactic dolasetron or droperidol vs rescue therapy in the prevention of PONV in ambulatory gynecologic surgery. Can J Anesth 1999;46:536–43.
- Tang J, Watcha MF, White PF. A comparison of costs and efficacy of ondansetron and droperidol as prophylactic antiemetic therapy for elective outpatient gynecologic procedures. Anesth Analg 1996;83:304–13.
- Watcha MF, Smith I. Cost-effectiveness analysis of antiemetic therapy for ambulatory surgery. J Clin Anesth 1994;6:370–7.
- Domino KB, Anderson EA, Polissar NL, Posner KL. Comparative efficacy and safety of ondansetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting: a meta-analysis. Anesth Analg 1999;88:1370–9.
- Helmy ŠAK. Prophylactic anti-emetic efficacy of ondansetron in laparoscopic cholecystectomy under total intravenous anaesthesia: a randomised, double-blind comparison with droperidol, metoclopramide and placebo. Anaesthesia 1999;54:266-71.
- Fujii Y, Toyooka H, Tanaka H. Prophylactic anti-emetic therapy with granisetron, droperidol and metoclopramide in female patients undergoing middle ear surgery. Anaesthesia 1998;53:1165–8.

- Tramer MR, Reynolds DJM, Moore RA, McQuay HJ. Efficacy, dose-response, and safety of ondansetron in prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized placebo-controlled trials. Anesthesiology 1997;87:1277–89.
- 34. Graczyk SG, McKenzie R, Kallar S, et al. Intravenous dolasetron for the prevention of postoperative nausea and vomiting after outpatient laparoscopic gynecologic surgery. Anesth Analg 1997;84:325–30.
- 35. Korttila K, Clergue F, Leeser J, et al. Intravenous dolasetron and ondansetron in prevention of postoperative nausea and vomiting: a multicenter, double-blind, placebo-controlled study. Acta Anaesthesiol Scand 1997;41:914–22.
- Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. Anesth Analg 2000;90:186–94.
- 37. Janknegt R, Pinckaers JWM, Rohof MHC, et al. Double-blind comparative study of droperidol, granisetron and granisetron plus dexamethasone as prophylactic anti-emetic therapy in patients undergoing abdominal, gynaecological, breast or otolaryngological surgery. Anaesthesia 1999;54:1059–68.
- Splinter WM, Rhine EJ. Low-dose ondansetron with dexamethasone more effectively decreases vomiting after strabismus surgery in children than does high-dose ondansetron. Anesthesiology 1998;88:72–5.
- 39. Fujii Y, Saitoh Y, Tanaka H, Toyooka H. Combination of granisetron and droperidol in the prevention of nausea and vomiting after middle ear surgery. J Clin Anesth 1999;11:108-12.
- 40. **Bugedo G, Gonzalez J, Asenjo C, et al.** Ondansetron and droperidol in the prevention of postoperative nausea and vomiting. Br J Anaesth 1999;83:813–4.
- 41. Pueyo FJ, Carrascosa F, Lopez L, Iribarren MJ, Garcia-Pedrajas F, Saez A. Combination of ondansetron and droperidol in the prophylaxis of postoperative nausea and vomiting. Anesth Analg 1996;83:117–22.
- Eberhart LHJ, Seeling W. Droperidol-supplemented anaesthesia decreases post-operative nausea and vomiting but impairs post-operative mood and well-being. Eur J Anaesth 1999;16:290–7.
- 43. Lim BSL, Pavy TJG, Lumsden G. The antiemetic and dysphoric effects of droperidol in the day surgery patient. Anaesth Intensive Care 1999;27:371–4.
- Foster PN, Stickle BR, Laurence AS. Akathisia following lowdose droperidol for antiemesis in day-case patients. Anaesthesia 1996;51:491–4.
- Henzi I, Walder B, Tramer MR. Metoclopramide in the prevention of postoperative nausea and vomiting: a quantitative systematic review of randomized, placebo-controlled studies. Br J Anaesth 1999;83:761–71.