Comparison of Inhalation of Isopropyl Alcohol vs Promethazine in the Treatment of Postoperative Nausea and Vomiting (PONV) in Patients Identified as at High Risk for Developing PONV

Joseph Pellegrini, CRNA, PhD, CAPT(ret), NC, USN
LT Jon DeLoge, CRNA, MSN, NC, USNR
LCDR John Bennett, CRNA, MSN, NC, USNR
Joseph Kelly, CRNA, MS, CDR(ret), NC, USN

Frequently, patients identified as high risk for postoperative nausea and vomiting (PONV) are treated prophylactically with intravenous (IV) ondansetron and postoperatively with IV promethazine. The purpose of this study was to determine if using an aromatic therapy of 70% isopropyl alcohol (IPA) would be more effective than promethazine in resolution of breakthrough PONV symptoms in groups of high-risk patients administered prophylactic ondansetron.

All subjects enrolled were identified as high risk for PONV, administered general anesthesia and a prophylactic antiemetic of 4 mg of IV ondansetron, and randomized to receive IPA or promethazine for treatment of breakthrough PONV. Demographics, verbal numeric rating scale (VNRS) scores for nausea, time to 50% reduction in VNRS scores, and overall antiemetic and incidence of PONV were measured.

The data for 85 subjects were included in analysis; no differences in demographic variables or baseline measurements were noted between groups. The IPA group reported a faster time to 50% reduction in VNRS scores and decreased overall antiemetic requirements. A similar incidence in PONV was noted between groups.

Based on these findings, we recommend that inhalation of 70% IPA is an option for treatment of PONV in high-risk patients who have received prophylactic ondansetron.

Keywords: Isopropyl alcohol, postoperative nausea and vomiting (PONV), promethazine, risk factors for PONV.

In the general surgical population, the risk of postoperative nausea and vomiting (PONV) is between 16% and 30%; however, this risk ratio is increased even further when certain factors are present that predispose a patient to PONV.[1-5] These risk factors include general anesthesia of more than 60 minutes' duration, female gender, nonsmoker, history of PONV, and history of motion sickness.[1-7] In fact, it has been noted that the incidence of PONV increases exponentially from 16% when no risk factors are present to as high as 87% when all risk factors are present.[1-9] Therefore, it has become routine in many anesthesia practices to screen patients preoperatively to identify the patients at high risk for PONV so that an aggressive management plan can be implemented to prevent or decrease the severity of PONV symptoms.

Most typically, this aggressive management plan involves the prophylactic administration of an antiemetic agent that works specifically on an area of the brain called the chemotaxic trigger zone (CTZ).[1-5] The CTZ, located in the area postrema of the brain, lacks a blood-brain barrier, thereby making it highly receptive to stimulation from specific neurotransmitters that have been shown to be integral in eliciting an emetic response.[1-5] These neurotransmitters include serotonin, dopamine, histamine, and acetylcholine.[1-5] Although a variety of agents can be administered prophylactically to prevent PONV, the agent most often used is the serotonin antagonist ondansetron, an antiemetic agent that has been shown to be highly effective in preventing PONV in a wide variety of patient populations, while still having a relatively low side-effect profile.[6-11]

Ondansetron, when used as a prophylactic agent, is routinely administered approximately 15 to 30 minutes before the conclusion of the surgical procedure. Studies have shown that the prophylactic administration of ondansetron results in a 50% to 80% reduction in PONV in groups of low-risk patients but only a 25% reduction in patients identified as high risk for PONV.[10-12] Because of this lack of effectiveness in preventing PONV in patients identified as high risk, the patients will often require a subsequent antiemetic for treatment, and one of the most common agents used to treat this breakthrough PONV is the antiemetic agent promethazine.[8,13]

Promethazine is a dopamine receptor blocking agent routinely administered because it has a rapid onset of

action (within 3-5 minutes) and a relatively long duration of efficacy (approximately 2-6 hours).[8] However, unlike ondansetron, which has minimal side effects, promethazine is commonly associated with sedation, dry mouth, and, in rare cases, hypotension.[8,13] Despite these side effects, many practitioners prefer promethazine to other traditional antiemetic agents because it can be used in the inpatient and outpatient settings. Promethazine is routinely administered by the intravenous (IV) route to a patient while in the hospital but is also available in oral and suppository forms for outpatient administration.[8,13] However, some patients report hesitancy to taking an oral antiemetic when they are nauseous; therefore, many practitioners prescribe the suppository form to avoid oral administration and because it can be easily self-administered by a patient in the home setting. Despite this, many patients still report hesitancy toward self-administration of a promethazine suppository and often report that the side effects following administration are unacceptable.[9,14] Therefore, anesthesia practitioners are continually seeking alternative antiemetic treatments that are highly effective in treating PONV, can be easily self-administered in any setting, and have a low side-effect profile.

A PONV treatment that seems to meet all of these criteria is the aromatic treatment of 70% isopropyl alcohol (IPA) that is administered by simply using a single alcohol prep pad. Research has shown that inhalation of IPA from a simple alcohol prep pad is easy to administer in the inpatient and outpatient settings, is highly effective in treating PONV, and is associated with no side effects.[15-17] However, all of the studies to date using IPA have been done only with patients who are not classified as high risk for PONV, and IPA has never been used in a patient population that has been prophylactically treated with ondansetron. Therefore, the purpose of this study was to investigate the efficacy of IPA vs promethazine in treating breakthrough PONV in groups of high-risk patients who have received a perioperative prophylactic dose of ondansetron.

Methods

All patients scheduled for general anesthesia of more than 60 minutes' duration and having 2 of the 4 individual risk factors for PONV, (female gender, nonsmoker, history of PONV or motion sickness) were approached for possible inclusion in this institutional review board–approved prospective study. Patients were excluded from participation if they reported a recent upper respiratory infection; documented allergy to IPA, ondansetron, promethazine, or metoclopramide; antiemetic or psychoactive drug use within 24 hours; inability to breathe through the nose; pregnancy; history of inner ear pathology; and/or taking disulfiram, cefoperazone, or metronidazole. Patients with a body mass index greater than 35 kg/m^2 also were excluded from the study. In addition, following enrollment, the data were excluded from analysis for subjects who required inpatient hospitalization for reasons not related to PONV.

Once inclusionary criteria were met, informed consent was obtained and demographic data were collected, including age, height, weight, gender, ASA class, body mass index, race, and surgical procedure. All subjects were then randomly assigned using a computer-generated random numbers process into a control or an experimental group. The control group was assigned to receive 12.5 to 25 mg IV promethazine for complaints of PONV in the postanesthesia care unit (PACU) and same-day surgery unit (SDSU) and by promethazine suppository self-administration following discharge to home. The experimental group was assigned to receive treatment of PONV by administration of inhaled 70% IPA.

In the preoperative holding area, all subjects received instruction on treatments, study requirements, and the home data collection tool. A baseline level of nausea was obtained on all subjects following informed consent using a 0 to 10 verbal numeric rating scale (VNRS) in which a score of "0" indicated "no nausea" and a score of "10" indicated the "worst imaginable nausea." Before transport to the operative suite, preoperative medications for anxiolysis and sedation were administered based on individual requirements and anesthesia providers' discretion using 0 to 5 mg of midazolam and/or 0 to 3 µg/kg of fentanyl IV. All preoperative medications administered were recorded.

On arrival to the operative suite, blood pressure, electrocardiographic, and pulse oximetry monitors were applied and a baseline set of vital signs was obtained and recorded. Anesthesia induction was facilitated with propofol, 1.5 to 2 mg/kg IV; lidocaine, 0 to 1 mg/kg IV; fentanyl, 0 to 5 µg/kg IV; and a neuromuscular blocking agent of the anesthesia provider's choice. Following induction, all subjects were endotracheally intubated, and, based on surgical requirements, an orogastric tube was inserted and stomach contents were evacuated. All orogastric tubes were removed immediately before extubation, and the use of an orogastric tube was recorded. Maintenance of anesthesia was achieved with isoflurane, desflurane, or sevoflurane in combination with oxygen, 50% or 100%, and nitrous oxide, 0% or 50%. An opioid of provider choice was used for maintenance of analgesia. The doses of all opioids administered during the perioperative period were later converted to morphine equivalents for analysis.[18] Approximately 15 to 30 minutes before extubation, all subjects received ondansetron, 4 mg IV. Neuromuscular blockade was reversed, if necessary, using neostigmine, 0.05 mg/kg, and glycopyrrolate, 0.1 mg/kg IV. All medications administered intraoperatively were recorded on the data collection tool. Additional information collected and recorded included the type of surgery, use of laparoscopic technique, total

estimated blood loss, total amount of IV fluids administered, estimated preoperative-postoperative fluid deficit, and anesthesia, surgical, and PACU times. All subjects were extubated before transfer to the PACU.

Following arrival to the PACU and SDSU, an admission VNRS for nausea was obtained and recorded. For the purposes of this study, *nausea* was defined as the subjective feeling of the urge to vomit, and *vomiting* was defined as the forceful expulsion of gastric contents. Each event had to be at least 60 seconds from any other event to be recorded as a separate event. In addition, VNRS scores were obtained and recorded at the first complaint of nausea, every 5 minutes following treatment for nausea for the first 30 minutes, and then every 15 minutes thereafter for 75 minutes after the event or until discharge from the PACU or SDSU. Nausea events were treated according to group assignment (IPA or promethazine).

Subjects in the control (promethazine) group received promethazine, 12.5 to 25 mg IV, at the first complaint of nausea in the PACU and SDSU; this dose could be repeated in 30 minutes for a maximum dose of 50 mg IV. For nausea that was refractory to promethazine, control subjects could receive metoclopramide, 10 mg IV every 15 minutes, not to exceed a total dose of 30 mg.

All subjects in the experimental (IPA) group received inhalation therapy using a commercially available 70% IPA pad (Webcol, Kendall Healthcare, Mansfield, Massachusetts). All subjects were instructed to remove the IPA pad from the protective covering, fold the IPA pad in half, hold the folded pad approximately 0.5 inches from their nares, and take 3 deep inhalations from the pad and discard it after use. This treatment could be administered by the PACU and SDSU nurses in the hospital setting or by the patient; however, subjects were instructed to self-administer their IPA treatments following discharge to home following the treatment regimen described above. The IPA treatments were ordered to be administered on an as-needed basis, up to a total of 3 separate applications (3 deep inhalations per application) every 15 minutes. For complaints of nausea refractory to IPA treatment (no resolution of PONV symptoms after 3 applications) or if a patient requested an antiemetic agent at any time, promethazine, 12.5 to 25 mg IV every 30 minutes was given, not to exceed a total dose of 50 mg IV, or metoclopramide, 10 mg IV every 15 minutes, not to exceed a total dose of 30 mg. These treatment protocols were the same in the PACU and SDSU settings. All pharmacologic treatments administered for nausea and VNRS score measurements were recorded.

Before discharge to home, all subjects were instructed to treat PONV symptoms based on their assigned group. The subjects in the promethazine group were instructed to treat any PONV using 25-mg promethazine suppositories every 6 hours on an as-needed basis. The subjects in the IPA group were instructed to use the folded IPA regimen as described in the hospital setting on an as-needed basis, up to a total of 3 separate applications. In addition, IPA subjects were also instructed that they could self-administer a 25-mg promethazine suppository for any PONV symptoms that were refractory to the IPA treatments or if they had exhausted the number of applications ordered and had not achieved resolution of PONV symptoms. All subjects were asked to record the time any antiemetic therapy was self-administered at home (IPA or promethazine), the number of nausea and emetic events, and the severity of nausea using the 0 to 10 VNRS scale before they self-administered any antiemetic therapy and every 15 minutes after initiation for a period of 30 minutes. Before discharge, all subjects were given a home data collection sheet to record these events and instructed that they would receive a telephone call by one of the investigators approximately 24 hours after surgery to obtain this information. In addition, during the telephone call, all subjects were asked to rate their level of satisfaction regarding their antiemetic therapy using the following scale: 1, totally dissatisfied; 2, somewhat dissatisfied; 3, somewhat satisfied; 4, satisfied; and 5, totally satisfied. All responses from the telephone interview were recorded on a data collection sheet.

Before initiation of this study, a power analysis was performed based on previous studies[15,16] that indicated that subjects in the IPA group would achieve a 50% reduction in their mean VNRS scores for nausea 15 minutes earlier than subjects randomized to receive promethazine treatment. By using an α of .05 and a β of .10, we determined that a sample size of 40 subjects per group would be required to determine if a difference between the groups existed. Factoring in a 20% attrition rate increased our sample size to 96 subjects (48 per group).

Statistical analysis was performed using SPSS software version 13.0 (SPSS Inc, Chicago, Illinois). Data analysis was accomplished using descriptive and inferential statistics. Demographic data and frequency data were analyzed using the χ^2 test and Pearson correlation. The VNRS scores and time to resolution were analyzed using a Student *t* test. Subject satisfaction scores, body mass index scores, and total promethazine requirements were analyzed using a Mann-Whitney *U* test. A *P* value of less than .05 was considered significant.

Results

A total of 96 subjects were enrolled, but 11 subjects were withdrawn, leaving a total of 85 subjects (IPA group, 42; promethazine group, 43) whose data would be included in the final analysis. Reasons for withdrawal included 4 subjects who received additional antiemetics intraoperatively (2 in each group), 1 subject inadvertently enrolled despite being scheduled for a nasal surgical procedure (IPA group), and 6 subjects who required postoperative inpatient hospitalization for reasons unrelated to PONV (3 in each group).

	Isopropyl alcohol (n = 42)	Promethazine (n = 43)	*P*
Age (y)	33.98 ± 10.9	37.09 ± 11.0	.052
Weight (kg)	75.43 ± 17.4	74.84 ± 13.3	.939
Median (range) body mass index (kg/m^2)	27 (22-34)	27 (21-33)	.947
Laparoscopy			
Total	21	20	.748
Gynecologic	14	11	.433
Gender			.763
Female	30	33	
Male	12	10	
Surgical time (min)	50.57 ± 34.32	57.63 ± 44.3	.416
Anesthesia time (min)	90.45 ± 39.5	101.1 ± 48.7	.272
PONV risk factors			.676
3 risk factors	24	26	
4 risk factors	12	9	
5 risk factors	6	8	
Time from PACU admission to PONV event (min)	90.9 ± 101.8	78.8 ± 76.7	.664
History of motion sickness			.723
Yes	26	25	
No	16	18	
Primary volatile agent used			.326
Desflurane	18	25	
Sevoflurane	22	16	
Isoflurane	2	2	
Opioid morphine equivalent			
Perioperative	24.05 ± 16.4	21.5 ± 9.1	.375
PACU	8.8 ± 5.7	9.3 ± 5.6	.775
SDSU	4.4 ± 2.5	4.1 ± 1.9	.736
Nitrous oxide use			.049[b]
Yes	25	16	
No	17	27	
Orogastric tube use			.668
Yes	16	19	
No	26	24	

Table 1. Description of Demographic Data, Preoperative Risk Factors, and Perioperative Information[a]

PONV indicates postoperative nausea and vomiting; PACU, postanesthesia care unit; SDSU, same-day surgical unit.

[a] Data are given as mean ± SD or number of cases unless otherwise indicated.

[b] Significant at $P < .05$.

No differences were noted between the groups in relation to demographic variables, surgical times, anesthesia times, use of laparoscopy, orogastric tube use, time to first PONV event from PACU admission, history of motion sickness, primary volatile agent used, or the total number of PONV risk factors present. A noted difference was in the use of nitrous oxide between groups: 59% of the IPA group received 50% nitrous oxide compared with 37% in the promethazine group ($P = .049$). However when a separate analysis of nitrous oxide use and PONV was performed, no significance could be found to indicate that nitrous oxide administration increased the incidence of PONV. No differences in the amount of opioids administered during the perioperative period were noted between groups ($P > .05$) (Table 1). No differences in fluid deficit, estimated blood loss, type of surgical procedure performed, total amount of IV fluid administered, or total hours without oral intake were noted between groups.

The overall incidence of postoperative nausea was similar between groups, with 76% (n = 32) of the IPA group reporting postoperative nausea compared with 60% (n = 26) of the promethazine group. ($P = .119$). Analysis

	Isopropyl alcohol (n = 42)	Promethazine (n = 43)	*P*
No. (%) of nausea events			
PACU	7 (17)	10 (23)	.448
SDSU	17 (42)	10 (23)	.088
Home	19 (45)	10 (23)	.019[a]
Median (range) promethazine requirements (mg)			
PACU	0	12.5 (0-25)	.002[a]
SDSU	12.5 (0-25)	25.0 (0-50)	.033[a]
Home	12.5 (0-25)	12.5 (0-25)	.214

Table 2. Incidence of Nausea Events and Median Doses of Promethazine Required Per Group Per Setting
PACU indicates postanesthesia care unit; SDSU, same-day surgical unit.
[a] Significant at $P < .05$.

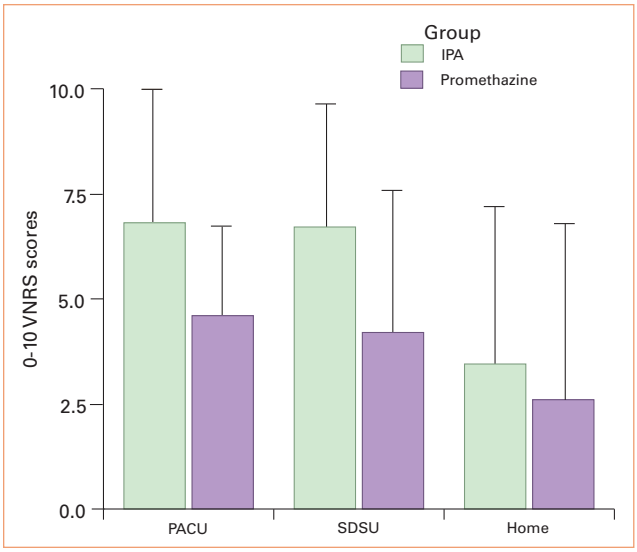

Figure 1. VNRS Scores on Initial Complaint Per Setting
VNRS indicates visual numeric rating scale; IPA, isopropyl alcohol; PACU, postanesthesia care unit; SDSU, same-day surgical unit.

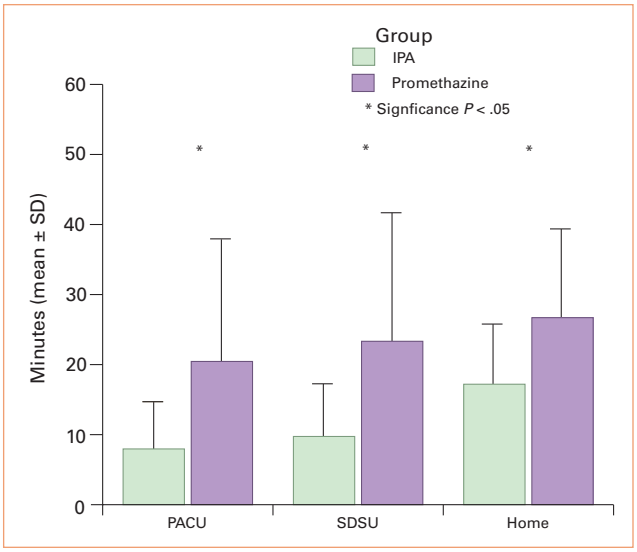

Figure 2. Time in Minutes to a 50% Reduction in VNRS Scores by Group Per Setting
VNRS indicates visual numeric rating scale; IPA, isopropyl alcohol; PACU, postanesthesia care unit; SDSU, same-day surgical unit.

of the incidence of nausea based on setting revealed that a higher incidence of PONV occurred in the IPA group in all settings but achieved significance only following discharge to home ($P = .019$). Promethazine was administered as the primary antiemetic agent in the promethazine group and as a rescue agent in the IPA group. Not surprisingly, the median dose of promethazine was higher in the promethazine group in all settings, achieving significance in the PACU and SDSU (Table 2). Analysis of the need for promethazine suppositories following discharge revealed that 23% (n = 10) of the promethazine group self-administered a promethazine suppository compared with only 7% (n = 3) of the IPA group ($P = .039$). No subject in either group required metoclopramide as a rescue agent in any setting. No differences in the VNRS scores were noted between groups on initial complaint of nausea in any setting (Figure 1). However, when time to 50% reduction in VNRS scores for nausea was analyzed, we noted a significantly faster time to a 50% reduction in VNRS scores in the IPA group compared with the promethazine group in the PACU ($P = .045$), SDSU ($P = .032$), and the home ($P = .017$) settings (Figure 2).

Emetic events were similar between the groups in the PACU (none), SDSU (IPA group, 3; promethazine group, 2) and in the home (5 in each group). Satisfaction with nausea control was similar between groups: both groups reported a median of 4 (satisfied) with the level of nausea control for the respective treatment regimens ($P > .05$). No subject who received IPA treatments exclusively reported any untoward side effects, whereas subjects who received promethazine as a primary or rescue treatment reported mild to moderate degrees of sedation and dry mouth; however, no subject required treatment for side effects.

Discussion

Postoperative nausea and vomiting continue to be persistent problems following general anesthesia. In our study, we used the risk factors for PONV identified by Koivuranta et al[1] that included the variables gender, smoking history, history of PONV, a history of motion sickness, and exposure to general anesthesia for more than 60 minutes to establish a risk of PONV. Koivuranta et al[1] reported that the relative risk of PONV for someone with 3 risk factors is 54%, with 4 risk factors is 63%, and with all 5 risk factors is 87%.

Based on these findings, we anticipated the overall incidence of PONV to be approximately 60%, given that the number of risk factors ranged between 3 and 5 in both groups. We anticipated this number to be decreased by a ratio of 25% to 42% following ondansetron administration. We were surprised to find that the overall incidence of PONV ranged between 61% and 76%, thereby indicating that ondansetron prophylaxis was not as effective as we hypothesized. However, analysis of the incidence of nausea in the PACU and SDSU revealed that the overall incidence of nausea was approximately 45% in both groups, indicating that ondansetron is limited in providing prophylaxis for the first few hours after surgery. Because of this limited range of effectiveness, it is common for patients at high risk for PONV to require subsequent antiemetic agents for the treatment of breakthrough PONV, which can often result in some significant side effects such as sedation and hypotension.

Another problem with traditional antiemetic agents is that they often cannot be administered easily in the home setting. In addition, the potential for side effects may place postoperative patients at risk. We chose IPA aromatic therapy as an avenue for investigation because previous research showed that it is effective in treating the symptoms of nausea and can be easily administered in the home setting.[15,16] However, these earlier studies were not performed on a high-risk patient population or in groups of patients already given ondansetron. In this study, we showed that IPA is effective in alleviating the symptoms of PONV and works very well in concert with ondansetron.

There has been some research that found that IPA is no more effective than other aromatic therapies or having the patient take several deep breaths of ambient air. For example, Anderson and Gross[19] reported that no difference in nausea scores was found among groups of patients asked to inhale peppermint, IPA, or saline, and they concluded that it was the simple act of taking a deep inhalation of air that was the inducement to relieve PONV symptoms rather than any specific aromatic properties. However, it was noted that this study was done on a very small group of patients (33 subjects), and the researchers did not have control over subsequent antiemetics administered during the perioperative and postoperative periods; therefore, it is difficult to ascertain the specific agent that facilitated the relief of PONV symptoms in the study. The findings of Anderson and Gross are contradicted in an earlier study by Langevin and Brown,[17] who compared the inhalation of IPA with placebo (saline) in a double-blinded study (30 subjects; 15/group). These investigators reported that administration of IPA resulted in a complete resolution of PONV symptoms in 80% of patients treated with IPA and that deep inhalation from a saline-soaked pad was totally ineffective in resolution of PONV symptoms, indicating that simply performing deep inhalations through the nose is not effective in alleviating symptoms of PONV.

Our study had some limitations. The SDSU staff was required to record VNRS scores every 5 minutes on complaint of PONV; therefore, we were forced to limit our subject enrollment to 1 or 2 subjects per day to ensure quality data collection. Also, in the home setting, we found there was a social stigma associated with the insertion of suppositories, and some patients reported hesitancy to use the suppository. We specifically chose a suppository over oral medication because it has also been noted that many patients are also hesitant to orally ingest a medication when they are experiencing nausea. It is unknown what overall effect this hesitancy may have had on the number of subjects who reported that they did not use the promethazine suppository as a rescue medication in the home setting. In retrospect, perhaps a better choice of an antiemetic for use as a rescue agent following discharge to home may have been an agent that does not require oral ingestion or suppository insertion, for example, sublingual ondansetron.

Although this study was designed using a unimodal approach to PONV prophylaxis, many practitioners report that more clinical effectiveness is observed when a multimodal antiemetic approach is used. The multimodal approach is used in an effort to optimize coverage on different receptors in the CTZ. While using this approach has been shown to be more effective in preventing PONV than using a single modal approach, it usually results in an increase in side effects.[6-9] Because of this, we are planning a future study in which we plan to provide IPA prophylaxis immediately before induction of general anesthesia in addition to the standard ondansetron prophylaxis 15 to 30 minutes before the conclusion of the surgical procedure. It is unclear where IPA works in relation to blocking the receptors in the CTZ. We hypothesize that it may possibly work on several sites simultaneously in the CTZ; therefore, IPA pharmacokinetics may already use a multimodal approach. However, we note that the clinical duration of IPA is limited; therefore, we propose that in an effort to optimize this multimodal approach, it may be best tested by incorporating ondansetron prophylaxis into the design as well. To date, only 1 study has been performed in which IPA was administered prophylactically, and the investiga-

tors reported that the inhalation of IPA was no more effective than the administration of granisetron but was more effective than no prophylactic treatment.[20] This study indicated that IPA prophylaxis was effective in preventing PONV, but the study used a small sample and administered the IPA following extubation, a different method than the one we are planning.

We believe that we clearly showed that IPA is as effective in treating PONV as promethazine in patients who have been identified as high risk for PONV, but it works considerably faster, works well in concert with ondansetron, and can be easily administered in any setting. Therefore, we are confident in recommending that IPA be considered a viable option to conventional antiemetic therapy in treating breakthrough PONV in groups of patients identified as high risk for PONV who have received perioperative prophylactic ondansetron.

REFERENCES

1. Koivuranta M, Läärä E, Snåre L, Alahuhta S. A survey of postoperative nausea and vomiting. *Anaesthesia.* 1997;52(5):443-449.
2. Eberhart LH, Högel J, Seeling W, Staack M, Geldner G, Georgieff M. Evaluation of the three risk scores to predict postoperative nausea and vomiting. *Acta Anaesthesiol Scand.* 2000;44(4):480-488.
3. Cohen MM, Duncan PG, DeBoer DP, Tweed WA. The postoperative interview: assessing risk factors for nausea and vomiting. *Anesth Analg.* 1994;78(1):7-16.
4. Haigh CG, Kaplan LA, Durham JM, Dupeyron JP, Harmer M, Kenny GN. Nausea and vomiting after gynaecological surgery: a meta-analysis of factors affecting their incidence. *Br J Anaesth.* 1993;71:517-522.
5. Kenny GN. Risk factors for postoperative nausea and vomiting. *Anaesthesia.* 1994;49(suppl):6-10.
6. Watcha MF, White PF. Postoperative nausea and vomiting: its etiology, treatment and prevention. *Anesthesiology.* 1992;77(1):162-184.
7. Apfel CC, Läärä 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(3):693-700.
8. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. *Drugs.* 2000;59(2):213-243.
9. Tong G. Postoperative nausea and vomiting: can it be eliminated? *JAMA.* 2002;287(10):1233-1236.
10. Claybon L. Single dose intravenous ondansetron for the 24-hour treatment of postoperative nausea and vomiting. *Anaesthesia.* 1994;49 (suppl):24-29.
11. Kovac AL, O'Connor TA, Pearman MH, et al. Efficacy of repeat intravenous dosing of ondansetron in controlling postoperative nausea and vomiting: a randomized, double-blind, placebo-controlled multicenter trial. *J Clin Anesth.* 1999;11(6):453-459.
12. Jones S, Strobl R, Crosby D, Burkard JF, Maye J, Pellegrini JE. The effect of transdermal scopolamine on the incidence and severity of postoperative nausea and vomiting in a group of high-risk patients given prophylactic intravenous ondansetron. *AANA J.* 2006;74(2): 127-132.
13. Dillon GP Jr. Clinical evaluation of promethazine for prevention of postoperative vomiting. *Am Pract Dig Treat.* 1957;8(10):1571-1575.
14. Scuderi PE, James RL, Harris L, Mims GR III. Multimodal antiemetic management prevents early postoperative vomiting after outpatient laparoscopy. *Anesth Analg.* 2000;91(6):1408-1414.
15. Winston AW, Rinehart RS, Riley GP, Vacchiano CA, Pellegrini JE. Comparison of inhaled isopropyl alcohol and intravenous ondansetron for treatment of postoperative nausea. *AANA J.* 2003; 71(2):127-132.
16. Cotton JW, Rowell LR, Hood RR, Pellegrini JE. A comparative analysis of isopropyl alcohol and ondansetron in the treatment of postoperative nausea and vomiting from the hospital setting to the home. *AANA J.* 2007;75(1):21-26.
17. Langevin P, Brown M. A simple, innocuous and inexpensive treatment for postoperative nausea and vomiting [abstract]. *Anesth Analg.* 1997; 84(suppl):S16.
18. Gordon DB, Stevenson KK, Griffie J, Muchka S, Rapp C, Ford-Roberts K. Opioid equianalgesic calculations. *J Palliat Med.* 1999;2(2):209-218.
19. Anderson LA, Gross JB. Aromatherapy with peppermint, isopropyl alcohol, or placebo is equally effective in relieving postoperative nausea. *J Perianesth Nurs.* 2004;19(1):29-35.
20. Teran L, Hawkins JK. The effectiveness of inhalation isopropyl alcohol vs granisetron for the prevention of postoperative nausea and vomiting. *AANA J.* 2007;75(6):417-422.

AUTHORS

Joseph Pellegrini, CRNA, PhD, CAPT(ret), NC, USN, is the former director of research, Navy Nurse Corps Anesthesia Program, Bethesda, Maryland. He is currently an associate professor, Nurse Anesthesia Program, University of Maryland, Baltimore, Maryland. Email: Pellegrini@son.umaryland.edu.

LT Jon DeLoge, CRNA, MSN, NC, USNR, is a staff nurse anesthetist at Naval Medical Center, Portsmouth, Virginia.

LCDR John Bennett, CRNA, MSN, NC, USNR, is a staff nurse anesthetist at Naval Medical Center, San Diego, California.

Joseph Kelly, CRNA, MS, CDR(ret), NC, USN, is a staff nurse anesthetist at University of Florida, Shands Medical Center, Jacksonville, Florida.

DISCLAIMER