Biphasic Dosing Regimen of Meclizine for Prevention of Postoperative Nausea and Vomiting in a High-Risk Population

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The purpose of this study was to determine if giving 50 mg of meclizine the night before and on the day of surgery would effectively reduce postoperative nausea and vomiting (PONV) for the entire 24 hours after surgery in patients identified as being at high risk for PONV. Subjects were randomly assigned to receive either 50 mg of oral meclizine (experimental group) or a placebo (control group) the night before and the day of surgery. All subjects were intravenously administered 4 mg of ondansetron before the conclusion of surgery. Seventy subjects (35 control; 35 experimental) were included in analysis.

In the placebo group we noted higher verbal numeric rating scale scores for nausea, a higher incidence of PONV, increased antiemetic requirements, and lower overall anesthesia satisfaction scores at all time intervals measured, compared with the experimental group, but the differences were not statistically significant until analyzed by postoperative setting. No difference in sedation or side effects was noted between groups.

Based on these results, we recommend that the administration of 50 mg of oral meclizine the night before and on the day of surgery be considered effective antiemetic prophylaxis in patients identified as having a high risk for PONV.

Keywords: Antiemetics, meclizine, ondansetron, postoperative nausea and vomiting.

Postoperative nausea and vomiting (PONV) continues to be a common complication after general anesthesia, with the incidence ranging from 17% to 87%.[1-5] It has been reported that approximately 72% of all patients undergoing surgical procedures list adequate PONV control as a principal concern, and other studies indicate that inadequate PONV control directly correlates with poor patient satisfaction.[3,6-8] Additionally, PONV complications remain one of the primary reasons for delayed discharge and/or unscheduled hospital admissions.[7-11] Studies show that PONV results in a significant increase in postoperative complications, including dehydration, electrolyte abnormalities, surgical-related pain, and wound dehiscence, thereby making PONV a concern for surgeons and anesthesia providers.[8,10]

There have been several factors identified that place a patient at greater risk for PONV: nonsmoker, female, history of motion sickness, history of PONV, and general anesthesia greater than 60 minutes.[3,7,11] It has been noted that the incidence of PONV increases exponentially from 17% when 1 risk factor is present to as high as 87% when all 5 risk factors are present.[3,7,11] Therefore, it has become routine in many anesthesia practices to specifically identify those patients at high risk for PONV so that an aggressive management plan of PONV prophylaxis can be implemented.[3,12-15] If at least 3 of the 5 risk factors are present, then these patients are identified as being at high risk for PONV.[11,12]

Most prophylactic PONV treatment regimens involve the use of antiemetic agents that work specifically to block the neurochemical activation of specific receptors located in areas of the brain called the chemoreceptor trigger zone and the vomiting center. Nausea and/or vomiting occurs when these receptors are stimulated by such neurotransmitters as serotonin, histamine, acetylcholine, and dopamine.[4] A variety of medications can be used to block transmission at these sites in the chemoreceptor trigger zone; one of the most commonly used antiemetic agents used for PONV prophylaxis is the serotonin receptor antagonist ondansetron. When administered as a sole prophylactic agent, ondansetron can reduce the incidence of PONV by as much as 50% in patients who have been identified as high risk for PONV[4-6]; it produces even greater efficacy when used in combination with another antiemetic agent that works on a different receptor site within the chemoreceptor trigger zone.[8,9] Some antiemetic agents typically used in combi-

nation with ondansetron include the common antiemetic agents droperidol, scopolamine, and metoclopramide.[15-18] Although these combinations are effective, they also can result in a fairly high incidence of undesirable side effects such as hypotension, somnolence, and respiratory depression; therefore, anesthesia providers are continually seeking alternative medication combinations that are both effective and possess a low side effect profile.[4]

One recent study has indicated that the administration of meclizine, an inexpensive H-1 antagonist, is effective in preventing and treating PONV in patients identified as high risk for PONV without causing a substantial increase in side effects.[14] This study analyzed the effect of using a combination of meclizine and ondansetron to prevent PONV in groups of high-risk patients. It found that prophylactic administration of meclizine given preoperatively the morning of surgery in combination with intraoperative IV ondansetron is effective in preventing PONV after discharge from the hospital but is less effective in preventing PONV in the immediate postoperative period. Therefore, the purpose of this study was to determine if the administration of meclizine the night before as well as the day of surgery in combination with intraoperative intravenous (IV) ondansetron is more effective in preventing PONV for the entire 24 hour postoperative period without a resultant increase in side effects.

Materials and Methods

• *Subjects.* Our institutional review board approved this prospective, randomized, double-blind, parallel-groups study. Patients having at least 3 of 5 risk factors for PONV (general anesthesia scheduled for greater than 1 hour, female gender, history of motion sickness, nonsmoker, and history of PONV) who were scheduled to undergo elective surgery with a likelihood of general anesthesia were approached for inclusion in the study. During the anesthesia evaluation in the preoperative clinic, a questionnaire detailing the 5 risk factors for PONV was given to all patients. Patients who answered "yes" to 3 or more risk factors were given an information sheet describing the objectives and parameters of this study, and then interviewed by investigators for possible inclusion in this study. Only patients greater than 18 years old and classified as ASA physical status I to III were approached for possible inclusion. Patients were excluded if they reported sensitivity to ondansetron or meclizine, had taken an antiemetic within 24 hours of surgery, or had a body mass index (BMI) greater than 35 kg/m^2. In addition, because meclizine is classified as a pregnancy category B drug by the US Food and Drug Administration, all women were asked if it was possible that they might be pregnant. A category B classification indicates that there is no evidence of risk to a human fetus or, if clinical trials are lacking, that animal studies do not show fetal risk; however, because the risk of teratogenicity in humans is not clear, patients who believed they might be pregnant were excluded from the study.[19]

• *Methods.* After inclusion criteria were met, written informed consent was obtained. Following informed consent, subjects were given a subject number and based on this subject number were randomly assigned into either the placebo or experimental group. Randomization was performed by the pharmacy using a computer-generated randomization process, and individual group assignment was not divulged to the subjects or investigators until conclusion of the study. All subjects were then issued the assigned study medication (placebo or meclizine) before the conclusion of the preoperative interview and instructed to self-administer the medications the night before surgery at bedtime but no later than midnight.

The study medication was prepared before initiation of this study by the pharmacy, which created 88 "bubble packs," each containing 2 capsules of either 50 mg of meclizine or placebo. These bubble packs were specifically designed by the pharmacy to ensure that each capsule looked alike and to ensure that both investigators and subjects were blind to the actual contents until the conclusion of the study. The pharmacy maintained a master list as to the actual contents of the capsules. The blue capsules were used because no suitable placebo could be found that identically matched the meclizine tablets. Along with the bubble pack, the subject received a detailed instruction sheet instructing them to ingest the contents of the capsule from the pack the night before surgery, either right before they retired for the evening or no later than midnight, whichever time came first.

In addition, baseline measurements were obtained in the preoperative clinic, which included demographic data (age, height, weight, BMI, and ethnicity/race) and a baseline nausea score. For this score, subjects were asked to rate their level of nausea using a 0 to 10 verbal numeric rating scale (VNRS) with 0 equating to "no nausea" and 10 equating to "the worst imaginable nausea." Also, a baseline sedation score was obtained using a 3-point ordinal sleepiness scale in which a score of 1 indicated "extremely sleepy—barely able to keep eyes open"; 2, "sleepy but easily aroused"; and 3, "awake and alert." All preoperative clinic information was recorded on a data collection sheet.

The evening before surgery, all subjects were contacted by phone to remind them to take the prescribed study medication. Subjects were instructed to note the time they took the study medication and report this time to the investigator on the morning of surgery. They were also given an opportunity to ask any final questions regarding the study. It was again stressed to women that meclizine is a category B medication. If subjects believed they may have become pregnant or had any other concerns at the time of the telephone interview they would have been instructed to withhold taking the medication; however, no subjects expressed these concerns.

On the morning of surgery, preoperative VNRS and sleepiness scale scores were obtained before the administration of the second "bubble pack" medication in the preoperative preparation area. The second "bubble pack" was verified by the investigators before administration to match the subject number assigned to the subject to ensure that the same medication (placebo or meclizine) matched the medication they self-administered the night before surgery. This second study medication was administered with a sip of water approximately 30 to 45 minutes before transport to the operative suite. The time of the second study medication administration was recorded on the data collection sheet, and this time was designated as time-zero (T_0) and used as an anchor to facilitate time interval measurements for the study. Following the second dose, subjects were then transferred to the preoperative holding area, where an IV line was placed in an extremity and an infusion of lactated Ringer's solution was administered at a rate of 100 mL/h. Based on provider preference or subject needs, all subjects were allowed to receive midazolam, up to 5 mg, and/or fentanyl, up to 2 µg/kg IV, for anxiolysis or sedation. The time, dose, and route of all medications administered in the preoperative area were recorded.

On the subject's arrival to the operative suite, routine monitoring devices—noninvasive blood pressure, electrocardiograph, end-tidal carbon dioxide, and pulse oximetry—were placed, and baseline vital signs were recorded. A standardized anesthesia induction was performed using fentanyl, up to 5 µg/kg IV; lidocaine, up to 1 mg/kg IV; propofol, 1.5 to 2 mg/kg IV; and a neuromuscular blocking agent of the provider's choice. Following induction, all subjects had an endotracheal tube (ETT) or laryngeal mask airway (LMA) placed. Anesthesia was maintained using isoflurane, desflurane, or sevoflurane in combination with nitrous oxide at a concentration up to 50% and oxygen at 50% to 100%.

The type of volatile agent used as well as the mean concentration used during the procedure were noted and recorded on the data collection sheet. Whether or not the patient underwent a laparoscopic procedure was also recorded on the data collection sheet since there may be more PONV associated with laparoscopy than with open procedures. Opioids were administered as per provider preference, and the total dose was recorded on the data collection sheet. Approximately 15 to 30 minutes before the conclusion of surgery, all subjects were administered 4 mg of IV ondansetron, as per study protocol. Residual neuromuscular blockade was antagonized using neostigmine, 0.05 mg/kg IV, and glycopyrrolate, 0.01 mg/kg IV.

Once operating room discharge criteria were achieved, the ETT or LMA was removed, and the subject was transported to the postanesthesia care unit (PACU). Total surgical time and anesthesia time, as well as the times and doses of all medications given intraoperatively, were noted and recorded on a data collection sheet. All analgesics administered intraoperatively were converted to morphine equivalents before analysis.

On the subject's arrival to the PACU, a 0 to 10 VNRS score for nausea was obtained and recorded for all subjects. In addition, a 0 to 10 VNRS score for nausea was obtained and recorded immediately before administration of any antiemetic, 30 minutes after antiemetic administration, and immediately before discharge from the PACU. Antiemetics ordered for treatment of PONV in the PACU included promethazine, 25 mg IV, every 30 minutes up to a total dose of 50 mg; ondansetron, 4 mg IV, every 30 minutes, up to a total dose of 8 mg; or metoclopramide, 10 mg IV, every 30 minutes, up to a total dose of 30 mg. Rescue antiemetic preference was left to the discretion of the anesthesia providers and/or PACU nursing personnel. All antiemetics administered were recorded on a data collection sheet. Occurrence of emesis was also recorded; emesis was considered a separate event if the interval from the previous emetic event was at least 1 minute. All analgesics administered for pain were recorded to include the type, dose, and route of administration and were converted to morphine equivalents before analysis.

Once it was determined the subject was suitable for transfer from the PACU, a 3-point sleepiness scale was performed and the total PACU time was recorded. Subjects were transferred from the PACU to either the same-day surgery unit (SDSU) or the inpatient ward. If the subject was discharged to the inpatient ward, the reason for inpatient transfer was noted, and all postoperative follow-up assessments were conducted on the ward.

Following transfer to the SDSU or inpatient ward, any incident of PONV was treated using the same medication regimen and the 0 to 10 VNRS time interval measurements as described for the PACU. Any incidence of emesis was also recorded as well as analgesics administered. Those subjects discharged from the SDSU underwent a 3-point sedation scale assessment, and the time of discharge was recorded on the data collection sheet.

Before discharge from the SDSU, subjects received a detailed instruction sheet regarding their home responsibilities for data collection. This sheet instructed the subject to record any incidents of nausea and emesis and to rate the severity at that time using the 0 to 10 VNRS score for nausea. The sheet also instructed them to record the time and type of any nausea treatments they self-administered at home. All subjects were instructed that they would receive a telephone call from one of the investigators to obtain this information approximately 24 hours after discharge from the hospital. For subjects on the inpatient ward, an instruction sheet was given to the inpatient nursing personnel asking them to record the same information as detailed on the home instruction sheet.

Approximately 24 hours after surgery, all subjects re-

	Meclizine group (n = 35)	Placebo group (n = 35)	*P**
Gender (No.)			
Female	16	17	.81
Male	19	18	
Age, y (mean ± SD)	37.4 ± 8.95	36.14 ± 11.06	.19
Weight, kg (mean ± SD)	81.1 ± 16.43	83.57 ± 18.61	.49
Height, cm (mean ± SD)	172.29 ± 10.7	173.23 ± 9.93	.69
Surgical time, min (mean ± SD)	72.23 ± 41.89	85.31 ± 49.22	.65
Anesthesia time, min (mean ± SD)	124.23 ± 49.43	147.34 ± 63.36	.36
SS scores (median) (range, 1-3)			
Preoperative	3	3	.74
Postoperative			
Discharge to PACU	3	3	.28
Discharge to SDSU	3	3	.45
24 hours	3	3	.72
PONV risk factors (No.) (range, 3-5)			
Median	4	4	.55
Female	17	16	.81
General anesthesia > 60 min	33	35	.15
Motion sickness	28	26	.57
History of PONV	26	24	.60
Nonsmoker	31	32	.69

Table. Demographic Data, Times for Surgery and Anesthesia, Median Scores for Risk Factors and Sedation Scale, and Data for Risk Factors

SS indicates sedation scale; PONV, postoperative nausea and vomiting.
*Significance < .05.

ceived a telephone call or were interviewed in person to obtain information regarding PONV incidence, severity, and treatment. All subjects were asked at that time to rate their level of sleepiness using the 3-point sleepiness scale for the first 24-hour period after surgery and to rate their level of satisfaction regarding the postoperative nausea control using a 1 to 5 Likert scale, in which a score of 1 indicated "totally dissatisfied"; 2, "dissatisfied"; 3, "moderately dissatisfied"; 4, "satisfied"; and 5, "totally satisfied." Before initiation of this study, all PACU, SDSU, and inpatient surgical ward staff were instructed on the goals and parameters of the study as well as their individual responsibilities regarding this study.

• *Data Analysis.* Inferential and descriptive statistics were used for data analysis. Demographic and frequency data were compared and analyzed using the Pearson χ^2 test and Student *t* test. A Student *t* test was used to analyze the difference between VNRS scores and analgesic and antiemetic requirements. A Mann-Whitney *U* test was used to analyze patient satisfaction scores and the 3-point ordinal sleepiness scale. A *P* value of <.05 was considered significant.

Before initiation of this study, a power analysis was performed based on previous research that reported a postdischarge incidence of nausea as approximately 32% in the placebo group and 10% in the meclizine group. Using these proportions, a 2-proportion power analysis was performed using an α of 0.05 and a β of 0.20 and revealed a need for approximately 40 subjects per group to achieve significance. Factoring in an attrition rate of 10%, this increased the necessary sample size to 44 subjects per group or 88 subjects for the total sample.

Results

A total of 88 subjects were enrolled, but 18 subjects were excluded from data analysis secondary to changes in the anesthetic plan (n = 5), surgical cancellation (n = 5), failure to adhere to study protocol (n = 7), or withdrawal per patient request (n = 1). A total of 70 subjects—35 controls and 35 in the experimental (meclizine) group—were included in the final analysis. No significant differences were demonstrated between the meclizine and control groups with regard to demographic variables (gender, age, height, and weight), risk factors for PONV, anesthesia and surgical times, and preoperative and postoperative sleepiness scale scores (Table) or in the number of laparoscopic procedures performed. No differences were noted between groups in relation to preoperative and intraoperative medications, volatile agents used, reversal agents, ETT and LMA use, nasal and oral gastric tube placement,

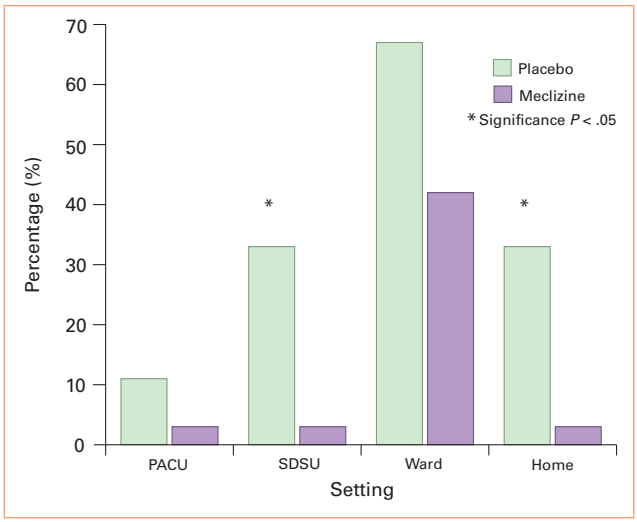

Figure 1. Complaints of Postoperative Nausea and Vomiting (PONV)

Higher incidence was noted of PONV complaints in the placebo group in all settings, achieving statistical significance in the same-day surgery unit (SDSU; $P = .018$) and after discharge to home ($P = .049$).

PACU indicates postanesthesia care unit; Ward, inpatient ward.

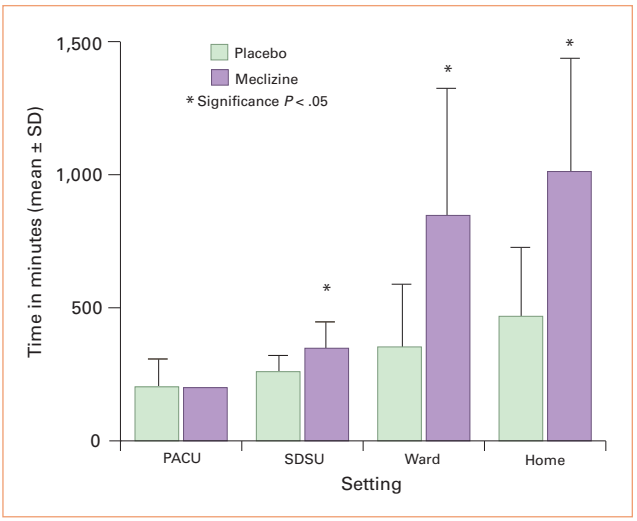

Figure 2. Time From Dosing to First Complaint of Postoperative Nausea and Vomiting (PONV)

Longer time was noted between groups to first complaint of PONV in all settings, achieving statistical significance in the same-day surgery unit (SDSU; $P = .036$), inpatient ward ($P = .044$), and after discharge to home ($P = .007$).

or the surgical procedure performed. No side effects (dry mouth, gastrointestinal disturbances, dysphoria) were noted in any subject in the meclizine group.

All subjects were admitted to the PACU after extubation; however, 15 subjects were admitted to the inpatient ward following discharge from the PACU, leaving 28 in the meclizine group and 27 in the placebo group for analysis in SDSU and in the home setting. All admissions to the inpatient ward were for reasons not related to PONV.

The overall incidence of PONV was noted to be higher in all settings in the placebo group compared with the meclizine group, achieving statistical significance in the SDSU and at home ($P < .05$; Figure 1). The VNRS scores for nausea were noted to be higher in the placebo group compared with the meclizine group at all time intervals except in the PACU setting (where 1 subject in the meclizine group reported nausea), but this difference achieved statistical significance only on admission to the SDSU and 30 minutes after treatment in the SDSU.

Time to first complaint of PONV was noted to be significantly longer in the meclizine group compared with the placebo group, achieving statistical significance ($P < .05$) in the SDSU, inpatient ward, and home settings (Figure 2). Time to second and third complaint of PONV was also measured in each setting, and we noted similar results as that for first complaints. However, the difference did not achieve statistical significance, because only 1 subject experienced a second episode of PONV in the meclizine group in the PACU, only 2 experienced a second episode in the SDSU and inpatient ward or home settings, and no subject in the meclizine group experienced a third episode of PONV in any setting. Second and third episodes were also noted to be small in the placebo group, with only 6 subjects reporting a second episode in the PACU and SDSU and only 2 subjects reporting a third episode in the ward or home settings.

The 2 antiemetic agents used to treat postoperative nausea were ondansetron and promethazine. Ondansetron was administered in only 7% (2) of the meclizine group compared with 37% (13) in the placebo group ($P < .05$). Promethazine was used in 18% (6) of the meclizine group compared with 44% (15) of the placebo group ($P < .05$). Median dose requirements for treatment were similar between groups, with both groups requiring a median dose of 4 mg of ondansetron and 25 mg of promethazine. In subjects who were discharged to home (excluding those admitted to the ward), the rate of nausea reported was 10% (3) in the meclizine group compared with 59% (16) of the subjects in the placebo-ondansetron group ($P < .001$). The incidence of vomiting and retching was similar between groups (2 subjects in the meclizine group vs 3 subjects in the placebo group).

Total time in the PACU and SDSU was similar between groups. The PACU time requirement was 50.86 ± 18.1 minutes in the meclizine group compared with 54.82 ± 32.6 minutes in the placebo group ($P = .535$). In the SDSU, an average of 226.93 ± 269.52 minutes was required before discharge in the placebo group compared with 167.83 ± 107.853 minutes in the meclizine group ($P = .269$).

Overall anesthesia satisfaction scores were significantly higher in the meclizine group compared with the placebo group; 85% (30) of the meclizine group reported a score of 5 (completely satisfied) compared with only 54% (19) of the placebo group ($P = .004$). No difference

in analgesic requirements in any setting was noted between groups.

Discussion

Earlier studies by Forrester et al[14] established that the prophylactic administration of meclizine before surgery in a high-risk population resulted in a profound decrease in PONV symptoms after discharge to home but was less effective in the immediate postoperative period. These authors hypothesized that the prophylactic administration of meclizine 30 to 60 minutes before induction of anesthesia did not allow enough time to establish a therapeutic blood level of meclizine for it to be effective immediately postoperatively. To test this hypothesis, we designed this study so that meclizine was administered not only in the immediate preoperative period but also at bedtime the night before surgery, in an effort to ensure that therapeutic blood levels of meclizine would be present to provide prophylaxis throughout the entire postoperative period. This study did validate this hypothesis in that we were able to demonstrate significant reductions in PONV between the groups throughout the entire postoperative period.

One of the concerns we had before initiation of this study was that the 2 doses of meclizine would result in a significantly higher level of sedation. As part of the design of the study, we incorporated a sleepiness scale to measure the degree of sedation or sleepiness and were surprised that the addition of meclizine did not result in a higher level of sleepiness. We attribute this to the relative spacing between the doses of meclizine (approximately 6 to 8 hours) and the low dose of meclizine used in this study (50 mg per dose). Sleepiness scales were performed at multiple time points in the preoperative and postoperative periods and failed to show a difference between groups. This result indicates the minimal effect that a total dose of 100 mg of meclizine administered using a biphasic process had on overall patient sensorium.

Another concern was that we were administering a dose of meclizine (or placebo) before obtaining a urine sample on the day of surgery for a pregnancy test. Meclizine is considered safe by many practitioners to administer during pregnancy, although its safety during pregnancy hasn't been definitively established by any controlled clinical trials; therefore, we excluded women who thought they were pregnant from inclusion in this clinical trial. No positive pregnancy tests were noted on any subject before surgery. In addition, we took special precautions to inform each prospective female subject that it is undetermined what effect meclizine has on a developing fetus by emphasizing this information both orally and in the written format before obtaining the informed consent.

One area that proved to be problematic in this study was the high rate of attrition that we encountered. A total of 18 subjects had to be excluded from the study for various reasons, which included failure to adhere to protocol (patients did not take their prescribed medication of meclizine or placebo the night before surgery despite receiving a telephone call to remind them), surgical cancellation, and patient's change of mind. In the cases in which the surgery was canceled, all these patients did take their prescribed medication regimen the night before surgery and were not administered a second dose on the day of surgery. The patient who decided to withdraw from participation did not take her medication and was administered general anesthesia and prophylactic antiemetic therapy that did not include meclizine. The 5 patients who were excluded because of a change in their anesthetic management were patients who informed the investigators either during the preoperative telephone interview or on the day of surgery that they wanted a regional anesthetic technique as opposed to general anesthesia. All subjects included in analysis received general anesthesia for their surgical procedure. If they reported a desire for regional anesthesia during the telephone conversation the night before surgery, they were instructed to withhold taking their medication "bubble pack." If they made the decision for regional anesthesia on the morning of surgery after they had already taken the medication in the "bubble pack," they did not receive the second dose on the day of surgery. Despite this high rate of attrition, we believe that the sample size was adequate to support our original hypothesis because those that received the meclizine had a significantly lower incidence and severity of PONV in the postoperative period.

An intent-to-treat analysis was not conducted on those subjects that dropped out of this study because the original intent of the study design was altered significantly in this small cohort of patients and they were often administered medications other than those used in our study. Therefore, it was too difficult to perform a comparative analysis.

The hospital setting in which this study was performed was a medium-sized military treatment facility that provides care to military personnel, their dependents, and retirees. As such, many surgeries that begin as scheduled outpatient procedures are changed to inpatient procedures after surgery. A total of 15 subjects in our study required inpatient hospitalization after surgery for various reasons. These reasons included the surgeon's unwillingness to return the patient to a small naval vessel where the subject could not be adequately monitored for the first 24 hours after surgery (11 subjects), lack of transportation home (1 subject), and need for extensive postoperative analgesia (2 subjects). No patient was admitted because of PONV.

Because this study was designed to ascertain the efficacy of treatment in the outpatient setting, these inpatients were not included in the SDSU data (because none were admitted to the SDSU) nor the home data, therefore

requiring a separate analysis. Despite this, a similar trend in the outcome variables was noted between the treatment groups. The meclizine group had a lower incidence of PONV, lower antiemetic requirements, lower VNRS scores, and higher patient satisfaction scores, thereby indicating that prophylactic meclizine may also be of some utility on patients admitted to an inpatient unit after surgery. These inpatients were included in the overall analysis for comparisons between the groups.

Another limitation we found with this study is that the population of subjects used was a young, healthy, active-duty military population or their dependents. It is unclear whether similar results would be obtained if this study were repeated using a nonmilitary, older population of patients.

Data analysis of the first report of PONV at home was consistent with past findings.[14] In the study by Forrester et al,[14] they reported an overall incidence of nausea as 10% in the meclizine group and 32% in the placebo group. In our study we found a similar overall incidence of nausea of 10% in the meclizine group but an increased incidence of nausea overall of 59% in the placebo group. When we excluded those subjects that were admitted to the inpatient ward, it increased the ratio of nausea to 14% in the meclizine group and decreased the ratio of nausea to 49% in the placebo group. However, these results were still consistent with what Forrester et al reported in their initial study

Our study did have some notable differences from that of Forrester et al.[14] In our study, subjects in the meclizine group were found to have a time to first report of PONV at home of 1,011.67 + 355.39 minutes compared with 737.2 + 303.0 minutes reported by Forrester et al. We believe that our increased nausea-free period may be directly related to our biphasic dosing protocol so that subjects who received meclizine were able to establish and maintain therapeutic blood levels before any noxious stimuli. The median time between the doses of meclizine was between 6 and 8 hours, which corresponds to the reported half-life of meclizine of approximately 6 hours. Given that the bioavailability of meclizine efficacy is 24 hours,[19] these patients received more substantial prophylaxis using this biphasic administration regimen than when meclizine was administered as a one-time dose in the immediate preoperative period. In addition, we concluded that the concomitant administration of ondansetron during the intraoperative period provided a greater degree of PONV prophylaxis in our experimental group because ondansetron works on a different receptor site (5-HT^3) in the chemoreceptor trigger zone than the meclizine, thereby providing the benefits of multimodal prophylaxis. Despite this combination of antiemetic agents, we noted that no patient experienced any significant side effects, indicating that this combination of agents is not only effective but also safe to use in patients who are at high risk for PONV.

In addition, we designed this study to include all types of surgical procedures in which general anesthesia was used in this high-risk population of patients. Using a population of patients undergoing a wide variety of surgical procedures made this treatment regimen more generalizable to the population of high-risk PONV patients typically seen in anesthesia practices.

Finally, it was noteworthy that those subjects administered the meclizine reported significantly higher overall satisfaction scores with their anesthetic regimen than those administered placebo. Given that PONV is one of the most frequent complaints of patients after surgery and that patient satisfaction is a metric that is closely scrutinized by institutional administration, the addition of meclizine prophylaxis described in this study could be used as a treatment regimen to decrease overall anesthesia-related adverse events.

Conclusion

Because of the large number of subjects who attrited from the study, we recommend further investigation with a larger sample size, especially since many of the results did not reach statistical significance. However, based on the findings of this study, we recommend that anesthesia practitioners should consider administration of 50 mg meclizine the night before and on the day of surgery using general anesthesia to patients who have been identified as high risk for PONV, to decrease the incidence and severity of PONV and to increase overall patient satisfaction with their anesthesia experience.

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