



# Comparison of ondansetron, dimenhydrinate versus placebo as PONV prophylaxis for outpatient gynecological laparoscopy

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## Abstract

This is a study comparing ondansetron, dimenhydrinate versus placebo as PONV prophylaxis for outpatient gynecologic laparoscopy. Postoperative nausea and vomiting (PONV) is very common following ambulatory gynecological laparoscopy. Prophylactic antiemetic therapy if safe, effective and affordable may reduce the incidence of PONV, expedite hospital discharge and improve patient satisfaction. After institutional review board approval, informed written consent was obtained from 87 ASA I–II women undergoing ambulatory gynecological laparoscopy. In a random and double blind fashion the women were divided into three groups receiving either ondansetron 8 mg, dimenhydrinate 50 mg or placebo. A standard anesthetic technique with propofol, fentanyl, mivacurium, nitrous oxide and isoflurane was used. Measurements of nausea, emesis, pain, drowsiness, and satisfaction and recovery milestones were recorded. Psychomotor recovery was evaluated using p deletion and digit symbol substitution (DSS) test. There was no difference in the groups with respect to demographic data. Dimenhydrinate prolonged immediate recovery and impaired psychomotor recovery, but there was no difference in postanesthesia care unit (PACU) or hospital discharge. The incidence of PONV was minimal. The visual analogue score (VAS) for nausea was only 1 on a scale from 0–10 cm in all groups. Only one patient in the placebo group experienced PACU emesis. The incidence and severity of PONV was so low, even in the placebo group that the use of prophylactic antiemetic therapy cannot be justified. © 1999 Elsevier Science B.V. All rights reserved.

*Keywords:* Ondansetron; Dimenhydrinate; Laparoscopy; Ambulatory; PONV

## 1. Introduction

Post operative nausea and vomiting (PONV) has been described as ‘the big little problem’ [1]. PONV remains the most frequently encountered and most distressing problem in post anesthetic care [2,3]. Severe PONV may lead to delay in discharge from day surgical units, unplanned admission, increased costs, and decreased patient satisfaction [4]. The ideal antiemetic agent would be inexpensive, non-sedating and effective regardless of etiology. The agents we currently use are not universally effective, expensive (ondansetron 8 mg

\$ 34.40)<sup>1</sup> or have undesirable side effects (droperidol, dimenhydrinate, prochlorperazine).

PONV following laparoscopic procedures is reported at a rate of 27–65%, therefore it is frequently used as the surgical model [1,5–8]. Many studies of antiemetic therapy appear to have been intentionally designed to increase the likelihood of PONV in order to easily demonstrate an effect. These studies use barbiturates, opiates and inhalational agents, in nausea prone surgery and patients with a history of PONV. Risk factors include anesthetic technique, age, gender, and hormonal levels in women for PONV [3,9].

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<sup>1</sup> Data from Pharmacy London Health Sciences Centre.

Numerous antiemetic drugs have been studied in an effort to reduce these symptoms [7,8,10]. Dimenhydrinate is commonly used in Canada and elsewhere as an antiemetic but has not been widely studied [11,12]. Dimenhydrinate is a H<sub>1</sub> receptor antagonist related to diphenhydramine. It is used to treat motion sickness, and vestibular diseases. Dimenhydrinate as an antiemetic was described in the 1950's [13,14]. Currently our institution uses approx. 25 000 doses of this drug per year. Various studies have described the efficacy of dimenhydrinate [12,15,16]. Bidwai describes a 26% reduction in the rate of PONV compared to placebo [15].

Ondansetron a serotonin subtype-3 receptor antagonist has been found to be effective in the prevention and treatment of PONV [7,10,17–19]. Reduction of PONV has ranged between 20–30% depending on the dose of ondansetron utilized as compared to placebo in gynecologic laparoscopy [7,10]. The cost of a single dose of 50 mg of dimenhydrinate (\$ 0.42) is substantially less than a dose of ondansetron 8 mg (\$ 34.40). We prospectively studied the cost effectiveness of dimenhydrinate versus ondansetron as prophylactic antiemetic therapy for laparoscopic surgery.

## 2. Methods

After institutional review board approval, informed written consent was obtained from 87 ASA physical status I–II women scheduled for elective gynecologic laparoscopy. The study design was double blind and randomized with a placebo control group. Preoperatively patients were screened for PONV risk factors including day of menstrual cycle, previous PONV and motion sickness. Patients received a standard anesthetic. Anesthesia was induced with propofol. Intubation was facilitated using mivacurium. Immediately post induction subjects received either placebo, ondansetron 8 mg, or dimenhydrinate 50 mg intravenously. Randomization and preparation of study drugs were completed by the hospital pharmacy. Narcotic dose was restricted to fentanyl 100 µg before induction and patients were maintained using isoflurane and nitrous oxide and oxygen. Gastric suction was not performed.

Postoperative nausea, drowsiness and satisfaction were evaluated by a blinded observer using a 10 cm visual analogue scale (VAS). Objective data regarding emesis or use of a rescue antiemetic was also collected. Psychomotor recovery was evaluated using p deletion and digit substitution tests, administered preoperatively, then one hour and 2 h after PACU admission. Test scores were calculated as a percent of preoperative baseline measurements.

The following day, in a telephone interview, measurements were obtained using a verbal rating scale (VRS)

Table 1  
Demographic data

	Placebo	Dimenhydrinate	Ondansetron
Patients (#)	29	28	30
Age (years)	32 ± 7	33 ± 7	33 ± 6
Height (cm)	165 ± 8	165 ± 12	162 ± 16
Weight (kg)	68 ± 15	69 ± 12	68 ± 15
Surgery (min)	28 ± 16	22 ± 8	25 ± 24
Anaesthesia (min)	35 ± 19	28 ± 7	36 ± 25

from 0–10. Willingness to repeat the same antiemetic therapy and to pay for antiemetic drugs was also determined. Patients were asked how much they would pay for an antiemetic on a scale from \$ 0 to 50. Statistical analysis was performed using ANOVA for parametric data,  $\chi^2$  for non parametric data, and a *P* value of < 0.05 was considered significant. The power of the study was calculated to determine a 2 cm difference in VAS for PONV. This figure was chosen since symptoms should be reduced by at least 20% to justify prophylactic therapy.

## 3. Results

Demographic data was similar in all groups (Table 1), and there was no difference in PONV risk due to menstrual cycle, motion sickness or prior PONV. The incidence of PONV was similar (Table 2). Combining PACU and home scores for nausea, requirement of rescue antiemetic and emesis episodes did not show a statistically significant difference (*P* < 0.05) between the groups (Figs. 1 and 2). VAS scores for PACU nausea were the same for each group (1 ± 2). No difference could be demonstrated in measurements of pain, dis-

Table 2  
PONV

		Placebo	Dimenhydrinate	Ondansetron
Any nausea	Home	38	33	29
	PAUC	29	20	12
Antiemetic (% patients)	Home	17	15	11
	PAUC	19	8	8
Emesis (% patients)	Home	4	4	0
	PAUC	21	17	10
Satisfaction VAS (cm)	Home	9 ± 2	9 ± 1	9 ± 2
	PAUC	8 ± 2	8 ± 2	8 ± 2
Mean ± SD				
Would repeat (% patients)		90	92	100

## Nausea

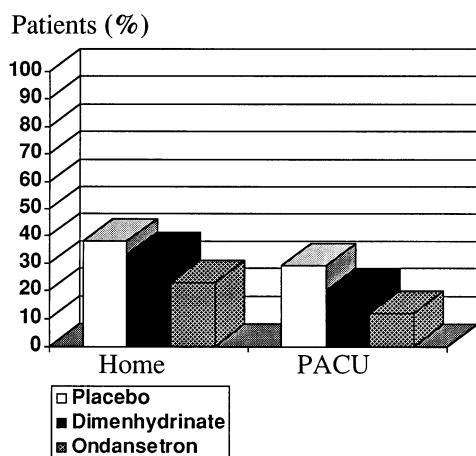


Fig. 1. The percentage of patients with any incidence of nausea at home or in the PACU. Patients were contacted by telephone interview 24 h post-operatively.

charge time, nursing care or supplies consumed. Immediate recovery from anesthesia and time to orientation were delayed ( $P < 0.05$ ) by dimenhydrinate (Table 3); and more patients in this group (Figs. 3 and 4 and Fig. 5) could not complete psychomotor tests and had lower scores on both the p deletion and DSS tests ( $P < 0.05$ ).

Analgesic requirement in PACU were similar in all groups, patients received an average of  $6 \pm 4$  mg intravenous morphine and two tablets of acetaminophen with codeine prior to discharge home. There was no difference in patient satisfaction or preference for the same future therapy (Fig. 6). Patients were willing to pay an average of  $\$32 \pm 17$  for antiemetic medication.

## Antiemetic Required

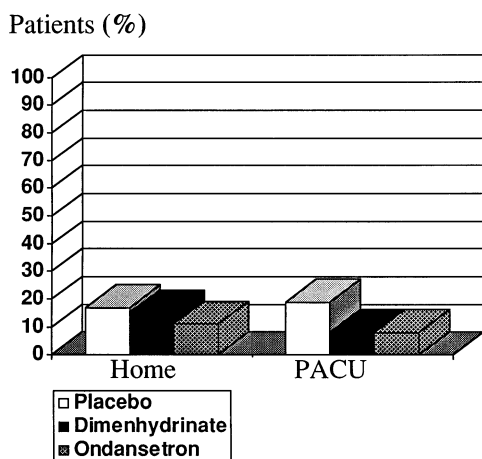


Fig. 2. The percentage of patients that required an antiemetic at home or in the PACU. Patients were contacted at home by telephone interview 24 h post-operatively.

Table 3  
Recovery profile

	Placebo	Dimenhydrinate	Ondansetron
Extubation (min)	$4 \pm 3$	$6 \pm 4$	$5 \pm 2$
Eyes open (min)	$5 \pm 4$	$8 \pm 5^*$	$5 \pm 3$
Oriented (min)	$7 \pm 4$	$12 \pm 8^*$	$8 \pm 4$
PAUC time (min)	$56 \pm 17$	$57 \pm 14$	$54 \pm 20$
Discharge (min)	$205 \pm 74$	$199 \pm 40$	$189 \pm 20$

\* Different from placebo,  $P < 0.05$ .

## 4. Discussion

This anesthetic protocol produced minimal PONV, even in the placebo group. Patient satisfaction (8/10 cm VRS) and willingness to repeat placebo therapy (90%) in future was very high. The cost of prophylactic ondansetron at \$34.00 is difficult to justify given the marginal and clinically insignificant benefits observed. While dimenhydrinate is a commonly used antiemetic, sedative properties make it undesirable for outpatient anesthesia.

Previous studies examining the efficacy of antiemetic therapy following outpatient laparoscopy have used barbiturates as the induction agent. This study is original in that it examines a commonly used antiemetic with a current and typical anesthetic technique. This makes our findings clinically relevant.

Propofol is commonly used as an induction agent in the ambulatory setting, and previous studies using this drug have reported rates of PONV in outpatient laparoscopy 27–50% [7,8]. Our incidence of PONV is similar to others using propofol as the induction agent. Studies using barbiturate induction for outpatient la

## Psychomotor Tests not completed

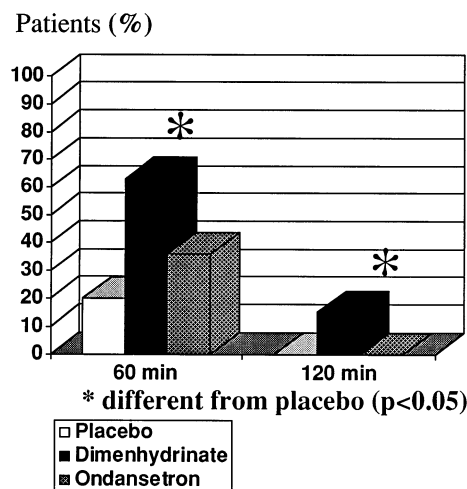


Fig. 3. The percentage of patients who were unable to complete psychomotor tests in PACU postoperatively. Measurements were made at 60 and 120 min. \*, denotes statistically significant compared to placebo at  $P < 0.05$ .

## P Deletion Test

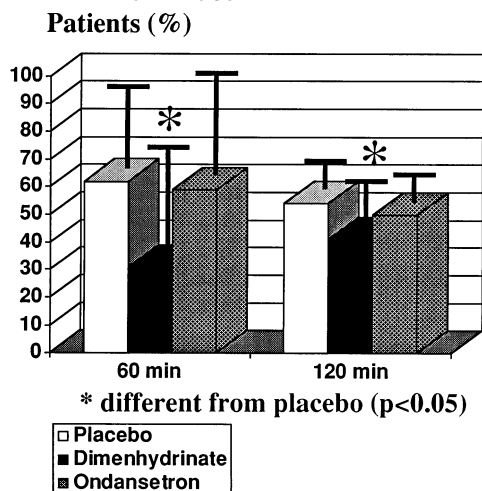


Fig. 4. P deletion tests were completed preoperatively to establish a baseline. The test was conducted at 1 and 2 h after PACU admission and calculated as a percent of baseline. Values are mean  $\pm$  SD and \* denotes statistically significant compared to placebo at  $P < 0.05$ .

paroscopy have a higher incidence of PONV [5,6,10]. Effectiveness of antiemetic therapy with thiopental has been demonstrated [5,6,10,17,19]. The value of prophylactic antiemetics when added to current clinical practice has not yet been demonstrated.

The study was designed with power adequate to determine a 2 cm difference in VAS for nausea. Previous studies have examined the objective presence of vomiting, any sensation of nausea or the use of a rescue antiemetic. This study is unique as it measures the severity of symptoms and not just the incidence of

any PONV. Patients were asked to subjectively rate severity of nausea. Overall nausea was minimal. Although some individual patients reported nausea it was not rated as distressing regardless of which drug they had received. Ondansetron and dimenhydrinate did not reduce the incidence or the severity of PONV.

Dimenhydrinate has some central nervous system depressant effects [20]. Therefore the study drug was given after induction of general anesthesia to blind the patient and anesthetist. Dimenhydrinate was shown to delay emergence from anesthesia and patients were less able to complete psychomotor tests after. While this did not affect PACU time or time to discharge from the hospital additional sedation without a significant reduction in PONV offers no clinical advantage. Previous studies have demonstrated the effectiveness of ondansetron as an antiemetic [5,8,18]. We examined the cost effectiveness of ondansetron versus placebo therapy in a high risk population. Despite a trend in reduced emetic episodes using ondansetron this was not statistically significant.

We found no benefit to prophylactic dimenhydrinate. In previous work on pediatric patients having strabismus surgery dimenhydrinate produced a 30% reduction in nausea and vomiting. This study examined pediatric patients having strabismus surgery with thiopental for induction of anesthesia [12]. The only recent adult study of prophylactic dimenhydrinate was conducted on patients receiving intravenous contrast material [16]. There was no benefit of prophylactic dimenhydrinate in preventing nausea and vomiting. This study did not use any sedative or anesthetic agents. Our study is unique as it examines the efficacy of a commonly used antiemetic that has not been investigated.

In this study the anesthetic protocol was designed to minimize PONV. The intraoperative narcotic dose was chosen to reflect current clinical practice in our institution, and to minimize the risk of opioid induced PONV. Despite the modest dose of intraoperative narcotic the pain scores and analgesic requirements in PACU were low and further justifies this as an appropriate dose of fentanyl. This anesthetic choice reflects an appropriate choice for outpatient laparoscopy.

## Digit Symbol Substitution

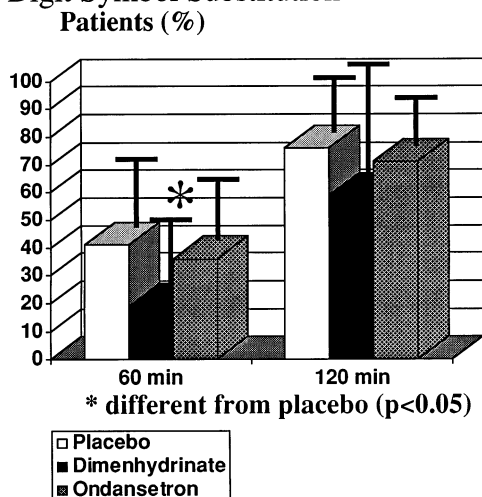


Fig. 5. DSS tests were completed preoperatively to establish a baseline. The test was repeated at one and two hours after PACU admission and calculated as a percent of baseline. Values are mean  $\pm$  SD and \* denotes statistically significant compared to placebo at  $P < 0.05$ .

## 5. Summary

PONV is a multifactorial problem, which may not have a singular therapeutic solution. PONV is an important complication and is distressing to our patients. Prior work has examined the efficacy of prophylactic antiemetic therapy. Further work should focus on the optimal anesthetic agents to avoid PONV and the best rescue agent should symptoms occur. In this study the anesthetic technique produced insufficient PONV to

## Satisfaction

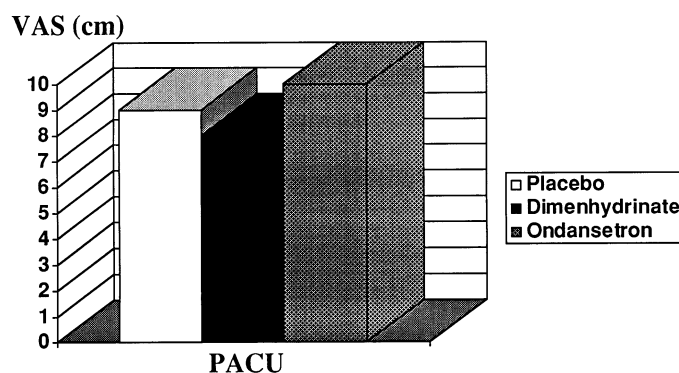


Fig. 6. Patients were asked to mark their satisfaction on a visual analogue scale from 0 to 10 cm. Values are mean  $\pm$  SD.

justify prophylactic use of antiemetic agents. With new anesthetic drugs the ‘big little problem’ may eventually become just a simple little problem after all.

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