Reduction of post-operative nausea and vomiting with the combination of morphine and droperidol in patient-controlled analgesia

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Purpose: To determine whether low doses of droperidol mixed with morphine in patient-controlled analgesia (PCA) would extend the duration of prophylaxis against postoperative nausea and vomiting.

Methods: Healthy women having elective open-abdominal gynaecological surgery consented to this double-blind, placebo-controlled study. Subjects were randomized to receive placebo, or 1 mg droperidol before induction followed by droperidol 0.0 (bolus group), 0.02 (0.02 group), or 0.04 (0.04 group) mg·mg⁻¹ of PCA morphine. Study endpoints included severity of nausea, episodes of vomiting and rescue antiemetic doses, pain, and sedation and were assessed at 1, 2, 4, 8, 12, 16, 20 and 24 hr postoperatively.

Results: Seventy-one subjects completed the study. The groups were similar in age, weight, surgical time, pain scores, and morphine used. The 0.04 group had lower mean visual analogue scale scores for nausea ($P < 0.05$ vs all other groups). The incidence of vomiting was lower in all treatment groups ($P < 0.05$ for all groups vs placebo). The 0.04 group had lower rescue antiemetic requirements than the bolus group ($P < 0.03$). Mean sedation scores were low in all groups but were increased with PCA droperidol ($P < 0.02$).

Key words

ANALGESICS: patient-controlled analgesia, morphine;
NAUSEA: antiemetics: droperidol, promethazine;
PAIN: perioperative;
SURGERY: gynaecological;
VOMITING: antiemetics: droperidol, promethazine.

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Conclusions: Droperidol 1 mg before induction of anaesthesia reduces postoperative vomiting. The addition of droperidol 0.04 mg·mg⁻¹ of PCA morphine further reduces (i) severity of nausea and (ii) rescue antiemetic requirements postoperatively. No clinically significant side-effects were attributed to this regimen.

Objectif: Établir si de faibles doses de dropéridol combinées à la morphine pour l'analgésie auto-contrôlée (PCA) peuvent prolonger la prévention antiémétique.

Méthodes: Des femmes en bonne santé soumises à une chirurgie gynécologique abdominale ouverte ont consenti à participer à cette étude en double aveugle et contrôlée avec placebo. Les patientes ont été réparties aléatoirement pour recevoir soit un placebo, soit dropéridol 1 mg avant l'induction suivi de dropéridol 0,0 (groupe bolus), 0,02 (groupe 0,02) ou 0,04 (groupe 0,04) mg·mg⁻¹ de morphine en PCA. Les données recueillies portaient sur la gravité des nausées, les épisodes de vomissements et les doses d'antiémétiques de sauvetage, sur la douleur et la sédation, après 1, 2, 4, 8, 12, 16, 20 et 24 de l'intervention.

Résultats: Soixante et onze patientes ont complété l'étude. Les groupes étaient identiques quant à l'âge, le poids, la durée de la chirurgie, les scores de douleur et la morphine administrée. Le groupe 0,04 présentait les scores moyens les plus bas sur l'échelle visuelle analogique pour la nausée ($P < 0,05$) vs tous les autres groupes). L'incidence des vomissements était inférieure pour tous les groupe traités ($P < 0,05$ pour tous les groupes vs placebo). Le groupe 0,04 avait des besoins moins importants d'antiémétiques de sauvetage que le groupe bolus ($P < 0,03$). Les scores moyens de sédation étaient bas dans tous les groupes mais augmentaient avec le dropéridol en PCA ($P < 0,02$).

Conclusion: Le dropéridol 1 mg avant l'induction diminue les vomissements postopératoires. L'addition de dropéridol 0,04 mg·mg⁻¹ à la morphine en PCA diminue encore plus (i) la gravité des nausées et (ii) les besoins d'antiémétiques de sauvetage postopératoires. Aucun effet secondaire important n'a été noté.

Postoperative nausea and vomiting (PONV) is a frequent and important complication of surgery and anaesthesia.^{1,2} Its overall incidence has been documented to be in the range of 20–30%,^{2,3} but may be as high as 60% in certain patient populations, such as women undergoing gynaecological surgery.^{3,4} Not only is PONV distressing for patients but, if left uncontrolled, it can lead to considerable morbidity including fluid and electrolyte imbalance, compromise of surgical sites, and aspiration.⁵

The aetiology of PONV is multifactorial and includes patient-related factors such as age, sex, obesity, gastroparesis, pain and the onset of oral intake, as well as the specific surgical procedure and the anaesthetic technique applied.^{2,3} The use of opioids by any route during the perioperative period is an important factor contributing to PONV.³ A number of prophylactic regimens have been described to reduce the incidence of PONV.³ Droperidol is a centrally acting dopamine receptor antagonist which is frequently administered at the time of anaesthesia. It has been shown to be effective in a range of doses, although the duration of action of a single bolus is limited to several hours.⁶

The delivery of opioid analgesics using patient-controlled analgesia (PCA) systems provides effective pain control with a high degree of patient satisfaction.^{7,8} However, this method of administration has not been found to reduce the incidence of nausea compared with fixed interval intramuscular injections.³ Recently, a number of investigators have evaluated the addition of droperidol to PCA morphine syringes.^{9–13} In this way, a small dose of droperidol is administered with each morphine bolus, matching its administration to the ongoing opioid requirements and extending the antiemetic effects beyond the period covered by a single bolus dose.

Barrow *et al.*¹¹ and Gan *et al.*¹² established a reduction in PONV over 24 hr with a perioperative 1.25 mg bolus of droperidol in patients using PCA. The majority of studies which assessed the combination of droperidol and morphine in PCA infusions found further reductions in PONV beyond that achieved by a single perioperative bolus dose of greater than 1.0 mg.^{9–11} However, considerable amounts of droperidol were used to achieve this outcome, with between 3.2 and 7.37 mg being administered in 24 hr.^{9–11} One investigator evaluated the use of lower doses of PCA droperidol (0.016 and 0.033 mg · mg⁻¹ morphine), documenting a decrease in vomiting and rescue antiemetic use, but not severity of nausea, compared with droperidol 0.5 mg bolus alone. However no placebo group was employed to demonstrate an effect of this low bolus dose. The side effects of droperidol are dose-related and include sedation, prolonged recovery, anxiety, restlessness and, rarely, extra-

pyramidal symptoms which have been identified up to 24 hr after the administration of bolus doses as low as 1.25 mg *iv*.^{14–16} It would therefore be relevant to determine whether lower PCA doses of droperidol provide similar reductions in PONV over a bolus dose alone.

The purpose of this study was to determine whether PONV would be reduced in patients receiving PCA morphine following a single 1.0 mg perioperative bolus of droperidol, with or without the addition of droperidol 0.02 or 0.04 mg · mg⁻¹ PCA morphine.

Methods

Approval for this randomized, double-blind, placebo-controlled study was granted by the Queen's University Research Ethics Board. All ASA class I or II patients between the ages of 18 and 70 yr who were scheduled for elective open-abdominal gynaecological surgery were assessed for inclusion in the study. Exclusion criteria included pregnancy or lactation, Parkinsonism, underlying gastrointestinal diseases including gastric dysmotility, a documented allergic reaction to any of the medications used, or the concurrent use of any antipsychotic, antihistaminic, or antiparkinsonian medication.

After obtaining informed written consent, subjects were randomized to one of four groups. Each patient was assigned one 3 ml preinduction syringe and two 60 ml PCA syringes. The placebo group received a preinduction syringe containing 0.9% saline and PCA syringes containing morphine 2.5 mg · ml⁻¹ alone. The three treatment groups each received a preinduction syringe containing 1.0 mg droperidol, and PCA syringes containing morphine with no droperidol (the bolus group), or morphine with droperidol 0.02 or 0.04 mg · mg⁻¹ PCA morphine (the 0.02 and 0.04 groups). All syringes were prepared to the same volume and blinded by the Department of Pharmacy Services.

The anaesthetic protocol began with the intravenous administration of the assigned preinduction syringe followed by 0.075 mg · kg⁻¹ morphine. Anaesthesia was induced with propofol (1.5–2.5 mg · kg⁻¹ *iv*) and maintained with 60% nitrous oxide in oxygen and isoflurane titrated to keep heart rate and blood pressure within 20% of baseline values. Endotracheal intubation was facilitated with succinylcholine (1.0 mg · kg⁻¹ *iv*). Vecuronium was titrated to effect with neuromuscular monitoring and the block was reversed at the end of anaesthesia with neostigmine (2.5 mg *iv*) and glycopyrrolate (0.4 mg *iv*). No additional opioids or premedications were used. Fluid management with Ringer's Lactate was based on the fluid deficit calculated before surgery, as well as ongoing requirements and blood loss.

Upon arrival in the Post Anaesthetic Recovery unit

TABLE I Assessment scales for pain and sedation

Scale	Pain (0–5)	Sedation (1–5)
0	no pain	
1	mild	wide awake
2	discomforting	drowsy
3	distressing	dozing intermittently
4	horrible	mostly sleeping
5	excruciating	only awakens with stimulation

(PAR), subjects were provided with an intravenous PCA pump and their assigned PCA morphine syringe. The initial PCA bolus dose was set at 2.0 mg morphine with a one minute lockout. This was administered by the PAR nurses as needed until patients were able to do so independently, after which the lockout was increased to eight minutes. Patients continued to use the PCA pump and syringes assigned throughout the 24 hr study period. A rescue antiemetic protocol consisted of promethazine 12.5–25.0 mg *im* every six hours as needed for any nausea that the subjects found to be distressing.

Data obtained for each subject included age, weight, duration of surgery, and total amount of morphine used over the 24 hr study period. Assessments of pain, sedation, nausea, number of episodes of vomiting, number of doses of rescue antiemetic, as well as any noted side effects were recorded by blinded nursing staff at 1, 2, 4, 8, 12, 16, 20 and 24 hr using a standardized assessment form. Patients had consented to be awoken for these assessments if necessary. Scales for pain and sedation are listed in Table I. The degree of nausea was indicated by the subjects on a 10 cm visual analogue scale (VAS) ranging from “no nausea” (0 cm) to “extremely severe nausea” (10 cm). Subjects were instructed to use the VAS to indicate the average intensity of nausea experienced over the previous four hours, so as to account for episodes which occurred between assessment periods.

The number of subjects required for this study was calculated to detect a 2.0 cm difference on the 10 cm VAS for nausea with a power of 80% at a 5% level of significance. Based on this, a minimum of 16 subjects was required for each group. Analysis of variance (ANOVA) was used to evaluate normally distributed continuous data including age, weight, duration of surgery, and the amount of morphine used. Incidence of vomiting, and need for rescue antiemetic doses were assessed with a chi-square test, or a Fisher's exact test when expected values were less than five. Nausea VAS scores, as well as episodes of vomiting and number of rescue antiemetic doses were analyzed with a one-way analysis of variance using a non-parametric method (Wilcoxon rank sum test or Kruskal–Wallis test). Sig-

nificance for all tests was considered for a *P* value of less than 0.05.

Results

Results are presented as mean $\pm$ standard deviation. A total of 80 patients were enrolled in the study over a four month period. Nine subjects were subsequently excluded because of failure of data collection during follow-up ($n = 4$), breach of anaesthetic protocol ($n = 2$), change or cancellation of surgery after enrollment ($n = 2$), or the lack of an available PCA pump following surgery ($n = 1$). The data completion rate for the remaining subjects was 97.4%.

One subject in the 0.04 group (#21) experienced severe unremitting vomiting requiring breach of the rescue antiemetic protocol. She was treated with more frequent promethazine doses than allowed in the protocol. In retrospect, she reported frequent pre-existing gastrointestinal symptoms suggesting a disorder of gastric motility, and a history of severe medication and anaesthetic-induced vomiting. Her mean VAS score for nausea (6.36) and total number of episodes of vomiting in 24 hr (23) were greater than three standard deviations from the means of her group (0.76 ± 1.49 , 1.7 ± 5.4 respectively). Therefore, the analysis was done with and without these outlier data. All results presented include subject #21 unless otherwise specified.

The groups were similar with respect to age, weight, type and duration of surgery (Table II). The average pain scores (placebo 1.95 ± 0.67 , bolus 1.1 ± 0.64 , 0.02 group 1.89 ± 0.80 , 0.04 group 1.98 ± 0.80) and the average amount of PCA morphine used over 24 hr (Table III) did not differ among the four groups. The mean amount of droperidol used per subject was 1.00, 2.53 ± 0.84 and 3.92 ± 1.12 mg for the bolus, 0.02 and 0.04 groups, respectively (Table III).

Sixty-three subjects (88.7%) recorded at least one VAS score with a value greater than zero and no differences were noted among groups. The severity of nausea in all groups was mild, with the mean VAS scores for each group being less than 2 out of 10. The 0.04 group exhibited a lower severity of nausea over the 24 hr period (0.76 ± 1.49) than the placebo (1.73 ± 1.33 , $P < 0.01$), bolus (1.30 ± 1.27 , $P < 0.03$) and 0.02 groups (1.24 ± 1.28 , $P < 0.05$).

Twenty-nine patients (40.8%) vomited one or more times during the study. All treatment groups had at least a 45% reduction in the incidence of vomiting compared with placebo ($P < 0.04$ for bolus group, $P < 0.05$ for 0.02 group, $P < 0.02$ for 0.04 group) (Table IV). The relatively large number of episodes of vomiting in the 0.04 group was primarily due to subject no. 21 who accounted for 23 of the 31 episodes of vomiting for the

TABLE II Subject demographics

	Control group	Bolus group	0.02 group	0.04 group
Number of subjects	17	17	19	18
Age (yr)	37.4 ± 8.7	42.9 ± 10.2	43.1 ± 11.6	41.2 ± 9.8
Weight (kg)	73.6 ± 12.9	81.0 ± 13.3	73.0 ± 17.5	71.2 ± 17.0
<i>Type of surgery</i>				
– hysterectomy ± oophorectomy	14	13	15	15
– ovarian and tubal procedures	3	4	4	3
Duration of surgery (min)(mean ± SD)	105.0 ± 22.9	128.2 ± 52.0	121.8 ± 26.4	117.9 ± 25.7

TABLE III Morphine and droperidol utilization

	Control group	Bolus group	0.02 group	0.04 group
Total PCA morphine (mg)	89.4 ± 32.8	74.8 ± 24.3	76.6 ± 41.8	73.1 ± 28.0
Total droperidol (mg)	0.0	1.0	2.53 ± 0.84	3.92 ± 1.12

(mean ± SD).

TABLE IV Incidence of vomiting and rescue antiemetic use

	Placebo group	Bolus group	0.02 group	0.04 group
Vomiting (> 0 episodes)	70.6 % (12/17)	29.4 % (5/17)	36.8 % (7/19)	27.8 % (5/18)
Rescue antiemetic (> 0 doses)	76.5 % (13/17)	58.8 % (10/17)	42.1 % (8/19)*	22.2 % (4/18)

**P* < 0.05 from placebo.†*P* < 0.05 from placebo and bolus.

FIGURE 1 Total episodes of vomiting over 24 hr. The boxes encompass the 25th to 75th percentile data for each group. The upper error bars represent the 90th percentile and the circles represent outliers beyond this point. As illustrated by the outlier symbol, one patient (#21) in the 0.04 group accounted for 23 of the 31 episodes of vomiting. **P* < 0.05 from placebo.

group (Figure 1). Even with these data included, all treatment groups showed a lower total number of episodes of vomiting as compared with the placebo

group (*P* < 0.05 for bolus group, *P* < 0.04 for 0.02 group, *P* < 0.03 for 0.04 group). There were no differences in incidence or episodes of vomiting among treatment groups (Figure 1).

Thirty-five patients (49.3%) requested at least one dose of the rescue antiemetic. There was a reduction in the incidence of rescue antiemetic use and the mean number of doses per assessment period with increasing concentrations of PCA droperidol (Table IV). The placebo group had a 76.5% incidence of rescue antiemetic use, the bolus group 58.8% (NS vs placebo), the 0.02 group 42.1% (*P* < 0.05 vs placebo), and the 0.04 group 22.2% (*P* < 0.002 vs placebo, *P* < 0.05 vs bolus). No difference was found between the 0.02 and 0.04 groups. The same pattern of results was found for the total number of rescue antiemetic doses administered (Figure 2). In the 0.04 group, a total of 10 rescue antiemetic doses were requested in 24 hr, seven of these by patient #21.

The range of the mean sedation scores for all groups over 24 hr was between 2–3 on a scale of 1–5 (i.e., “drowsy”–“dozing intermittently”). No differences were found among any of the three treatment groups (bolus 2.60 ± 0.50, 0.02 group 2.86 ± 0.63, 0.04 group 2.91 ± 0.49). Scores for the placebo (2.39 ± 0.60) and bolus groups were similar, however the scores for the 0.02 and

FIGURE 2 Total rescue antiemetic doses over 24 hr. The boxes encompass the 25th to 75th percentile data for each group. The error bars represent the 10th and 90th percentile and the circles represent outliers beyond this point. As illustrated by the outlier symbol, one patient (#21) in the 0.04 group accounted for 7 of the 10 rescue antiemetic doses requested. * $P < 0.01$ from placebo, † $P < 0.03$ from placebo and bolus.

0.04 groups were both higher than the placebo group ($P < 0.02$ and $P < 0.01$, respectively). No patients were found to be difficult to rouse with mild stimulation after discharge from the recovery room.

The following minor adverse effects were reported: pruritus ($n = 3$ in the bolus group); dizziness ($n = 1$ in the 0.04 group); flushing ($n = 1$ in the placebo group).

Discussion

Postoperative nausea and vomiting is a common problem in the gynaecological population; its incidence and severity varies with the type of surgery, anaesthetic technique and method of postoperative analgesia.^{1,3,4} Many antiemetic agents have been assessed for prophylactic and therapeutic use in the postoperative period. Droperidol is commonly administered perioperatively in an attempt to reduce PONV, although the optimal dose and timing of administration is unclear.¹⁷ Doses which have been found to be effective range from 0.25 to 5.0 mg *iv*, while failure has been reported with doses as high as 2.45 mg *iv*.¹⁷⁻²⁰ Despite these differing results, a recent review concluded that a prophylactic benefit is likely, even at relatively small doses.¹⁷

The duration of antiemetic effect from both *iv* and *im* bolus doses of droperidol has been found to be 6 to 12 hr.⁶ This is in contrast to its brief redistribution and elimination half lives of 10 min and two hours respectively,²¹ suggesting that its therapeutic benefit extends beyond its pharmacokinetic profile and that even minute

central nervous system levels exert a beneficial effect. Successful prophylaxis has been found with bolus doses given either at the onset or the conclusion of anaesthesia, although failure to reduce PONV has only occurred in studies using preinduction dosing.¹⁷ A direct comparison between these two dosing regimens has not been reported. The current study protocol included a group receiving only a single 1.0 mg preoperative bolus dose of droperidol and confirmed a reduction in the incidence and frequency of vomiting over the follow-up period in comparison with a placebo group.

The administration of opioids leads to nausea and vomiting by a combination of mechanisms which are thought to involve both the chemoreceptor trigger zone and vestibular structures.^{22,23} The management of postoperative pain with PCA infusions has become a standard of care in many institutions for gynaecological patients due to its high rate of patient satisfaction with rapid onset of relief and avoidance of intramuscular injections.^{7,8} However, the incidence of PONV secondary to the administration of opioids appears to occur as frequently with PCA infusions as with fixed interval *im* injections.³

Recently, a number of studies have assessed the benefit of combining an initial loading dose of droperidol with small boluses delivered by PCA pump, hypothesizing that the antiemetic effect would be prolonged when matched with ongoing opioid administration.⁹⁻¹³ Single perioperative 1.25 mg bolus doses of droperidol reduced PONV in patients using PCA morphine over 24 hr.^{11,12} In addition, most of these studies found further reductions in PONV when a single perioperative droperidol bolus of greater than 1.0 mg was supplemented with PCA droperidol in doses as low as 0.05 mg · mg⁻¹ morphine.⁹⁻¹¹ McKenzie *et al.*¹³ used the lowest doses published to date. He evaluated a reduced perioperative loading dose of 0.5 mg with and without PCA droperidol doses of 0.016 or 0.033 mg · mg⁻¹ morphine. Although he found a reduction in PONV with the addition of PCA droperidol, the lack of a placebo group precluded any conclusion that the bolus dose alone was beneficial. It is possible that the benefits gained by the PCA droperidol were only significant in that the perioperative bolus dose itself was ineffectual. Therefore to permit comparison with previous investigations,⁹⁻¹¹ the present study was designed to evaluate the effect of PCA droperidol doses which were less than 0.05 mg · mg⁻¹ morphine following a 1.0 mg perioperative bolus on PONV in healthy women undergoing open-abdominal gynaecological surgery over the first 24 hr of postoperative PCA use. The population that we studied would appear to be an accurate sample as the placebo group had a 71% incidence of vomiting which is similar

to that previously documented in women undergoing gynaecological surgery.^{3,4}

In a similar population to the present study, Williams *et al.*⁹ found a reduction in the incidence of nausea at 12 hr and a reduction in its severity at both 12 and 24 hr when droperidol 0.10 mg·mg⁻¹ PCA morphine was used after a bolus of 2.5 mg at the time of induction. Sharma *et al.*¹⁰ used lower doses and demonstrated a 50% overall reduction in the incidence of nausea over 24 hr, while Barrow *et al.*¹¹ established a reduction in the number of four-hourly assessments during which nausea occurred. In contrast, Gan *et al.*¹² found no difference in the incidence of nausea when droperidol 0.160 mg·mg⁻¹ PCA morphine was added to a 1.25 mg control bolus in subjects undergoing orthopaedic procedures. McKenzie *et al.*¹³ used the lowest doses published and found no change in the incidence or severity of nausea when a 0.5 mg bolus of droperidol was followed with or without droperidol 0.016 mg or 0.033 mg·mg⁻¹ PCA morphine.

The mean VAS nausea scores in the present study were quite low in all groups. However, many subjects still perceived their level of nausea as being distressing and uncomfortable, since vomiting and requests for rescue antiemetics occurred despite the low scores. This raises the question of the clinical importance of small differences in the VAS scores for nausea. The VAS has been validated for assessment of nausea in antiemetic trials of oncology patients receiving chemotherapy,²⁴ and adopted for use in the postoperative setting.⁹ Williams *et al.* used a VAS to assess severity of nausea with PCA droperidol and found similar results to the present study with mean scores less than 2 out of 10 in both groups.⁹ Despite the small range of scores documented by both of these studies, statistically significant reductions in severity were identified with the addition of droperidol to PCA morphine. This reduction in the severity of nausea also correlated with a reduction in the number of rescue antiemetic doses required in both studies, suggesting that small differences in mean VAS nausea scores may have a relatively large impact on patient comfort. However, the study by McKenzie *et al.* indicates that there is a minimum PCA dose of droperidol below which any such benefit may be lost.¹³ Therefore, it appears that droperidol 0.04 mg·mg⁻¹ PCA morphine following a 1.0 mg perioperative bolus dose is the minimum PCA dose that has been documented to produce a clinical reduction in the severity of nausea.

Similar variations in the incidence of vomiting were found in the previous studies. Patient controlled analgesia with droperidol and morphine following bolus doses of 1.25 and 2.50 mg of droperidol failed to reduce the incidence or frequency of vomiting in three of the stud-

ies.^{9,11,12} Gan *et al.* also found that droperidol 0.160 mg·mg⁻¹ PCA morphine alone was as effective as a single 1.25 mg bolus dose.¹² In contrast, Sharma *et al.* found a 100% reduction in the incidence of vomiting with PCA droperidol following bolus doses of 0.20 mg·kg⁻¹.¹⁰ McKenzie *et al.* demonstrated a 50% reduction in both the incidence and frequency of vomiting with the addition of either droperidol 0.016 or 0.033 mg·mg⁻¹ PCA morphine, although this benefit may have resulted due to the very small loading dose used (0.5 mg).¹³ Our study confirmed that a preoperative droperidol bolus of 1.0 mg reduces the incidence and frequency of vomiting compared with placebo, but that further reduction could not be obtained from the addition of droperidol to PCA morphine. Considering that the sample size of the study was calculated for the primary endpoint of severity of nausea, it is possible that an insufficient number of subjects was studied to demonstrate a significant difference in vomiting between the groups.

Previous studies have documented a 40–95% reduction in either the incidence or number of rescue antiemetics required.^{9–11,13} Gan *et al.* was the only group that found no reduction in the incidence of rescue antiemetic doses required when droperidol was added to the PCA morphine following a control bolus.¹² McKenzie *et al.* established a dose-response relationship for PCA droperidol with respect to both the incidence and frequency of rescue antiemetic doses provided.¹³ Our study also found a dose-response relationship in that the addition of droperidol 0.02 mg·mg⁻¹ PCA morphine only provided additional reduction in PONV compared with the placebo group, while the 0.04 group had a greater reduction compared with both the bolus and placebo group. The droperidol 0.02 and 0.04 groups were not different, again possibly due to the size of the study.

Finally, side effects attributable to doses of droperidol as used in this study appear to be rare. This study, as well as most previous investigations, noted an increase in the level of sedation with the addition of droperidol to PCA infusions, but not to an excessive degree.^{9,10,12} The mean level of sedation in the current study was less than 3 on a scale of 1 to 5 (i.e., "dozing intermittently") in all groups, and at least two of the assessment periods occurred during normal sleeping hours. No patient in any group complained of excessive sedation, nor were any found to be difficult to rouse with mild stimulation after discharge from the recovery room. Thus, although the difference reached statistical significance, it was not felt to be clinically important. Extrapyramidal signs have been described with bolus doses of droperidol as low as 1.25 mg *iv*, however none of the studies reviewed reported any such findings.^{14–16}

This study and most of those discussed above provide clinically relevant outcomes because women undergoing gynaecological procedures have a higher incidence of PONV than do many other surgical populations.^{3,4} The exclusion criteria limited the population to healthy women who were not pregnant or lactating and who did not have Parkinsonism or underlying gastrointestinal dysfunction. Age, weight, pain, duration of surgery and the amount of morphine used were similar between the groups, but other patient factors which might contribute to PONV such as timing of menses, anxiety, history of motion sickness, onset of oral intake and ambulation were controlled solely by the randomization process. The anaesthetic technique was standardized and comparable with other studies. Propofol was selected as the induction agent to eliminate the possible contribution of other induction agents to PONV. Propofol itself has been shown to cause little nausea, and indeed studies have suggested that it has an antiemetic effect.^{25,26} This may have contributed to the relatively mild severity of nausea experienced by most patients, including the placebo group.

One subject in this study experienced severe PONV which was not controlled by the rescue antiemetic regimen. As a result, the rescue antiemetic protocol was breached before completion of the 24 hr study period. This patient gave a history of frequent pre-existing gastrointestinal complaints and severe medication and anaesthetic-induced vomiting which was not elicited before entry into the study. Her mean VAS score for nausea and total number of episodes of vomiting were greater than three standard deviations from the means of her group (Figure 2). Although these data skewed the results, the conclusions from this study were statistically significant even with their inclusion.

In conclusion, droperidol administered as a 1 mg bolus prior to induction of anaesthesia reduced the overall incidence and frequency of vomiting in healthy patients receiving PCA morphine over 24 hr following open-abdominal gynaecological surgery. Droperidol 0.04 mg · kg⁻¹, but not 0.02 mg · kg⁻¹ PCA morphine, conferred an additional benefit in that it reduced both the severity of postoperative nausea and the necessity for rescue antiemetic administration. An increase in sedation was documented with the addition of droperidol to the PCA regimen, but this was not felt to be clinically important. No other clinically important side effects were attributed to this modality of antiemetic prophylaxis.

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