Adding Droperidol to Morphine Patient-Controlled Analgesia : Effect on Nausea and Vomiting†

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Abstract

This prospective, double-blind, randomized, controlled trial was performed to evaluate the antiemetic effectiveness and side effects of adding droperidol to morphine delivered *via* a patient-controlled analgesia (PCA) device in 94 women undergoing transabdominal hysterectomy with a standardized anesthetic regimen. They were randomly allocated to receive postoperative PCA as either bolus doses of morphine 1 mg or a combination of morphine 1 mg and 0.0625 mg droperidol with a lockout interval of 5 minutes and no continuous infusion. The incidence of nausea 6-18 hours postoperatively and 18-24 hours postoperatively was significantly lower in the morphine and droperidol group than in the morphine only group and its severity 2-6 hours, 6-18 hours, and 18-24 hours postoperatively was significantly lower. The number needed to treat to prevent nausea comparing the morphine only group at 6-18 and at 18-24 hours postoperatively were 4 and 4 (95% CI 2-27 and 2-11, respectively). The amount of morphine used 6-18 hours postoperatively in the droperidol group was lower than in the morphine only group. Although the incidence of vomiting and the amount of rescue antiemetics were lower in the morphine and droperidol group, the difference was not statistically significant. Postoperative pain scores were not different between the groups. No patients were oversedated. A series of extrapyramidal reactions were observed in one patient in the morphine and droperidol group. The drug and consumable item cost was not different between the groups. We conclude that droperidol added to morphine in PCA reduces nausea. The appropriate dose of droperidol should be further investigated to reduce the incidence of vomiting.

Key word : PCA, Droperidol, Morphine, PONV, Postoperative Analgesia, Nausea, Vomiting

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Postoperative nausea and vomiting (PONV) are distressing. The reported incidence of PONV varies from 8 per cent to 92 per cent[1-3]. The incidence is difficult to estimate because of the limited number of patients in each report and the methodological differences between studies. In the patients who received morphine by the conventional method, the incidence of PONV is around 4-52 per cent[4,5]. In those with PCA morphine, it varies from 21 per cent to 95 per cent[6-11]. Some patients were reluctant to press the PCA button to relieve their pain because they were afraid of becoming more nauseated or of vomiting. So they were not able to make the most of the PCA method to relieve their pain.

Droperidol is a potent antagonist of the dopamine (D_2) receptor at the chemoreceptor trigger zone. It mediates a good antiemetic action with a long duration. If the combination of droperidol and morphine in PCA reduces PONV, patients using PCA will get the most benefit from the analgesic action of morphine.

The objective of this study was to evaluate the effectiveness of droperidol in preventing PONV associated with PCA morphine and to observe its side effects.

MATERIAL AND METHOD

After institutional approval and obtaining informed written patient consent, we investigated 94 women (ASA physical status I or II) scheduled for elective transabdominal hysterectomy under general anesthesia in a prospective, double-blind, randomized, controlled trial. The exclusion criteria were asthma, history of allergy to morphine or droperidol, drug abuse, psychiatric problems, convulsions, parkinsonism, gastrointestinal symptoms, and chronic pain.

During the preoperative interview, the patients' age, weight, height, ASA classification, current pain score, the presence of nasal congestion, and any history of motion sickness or postoperative nausea and vomiting (PONV) after previous anesthesia were recorded. The patients were made aware that an intravenous (i.v.) antiemetic (metoclopramide 10 mg) would be available after operation on request or if they vomited. The concept and the use of PCA were explained to each patient.

In the operating room, each patient received general anesthesia with routine monitoring, including automated blood pressure monitoring, ECG, and pulse oximetry. Every patient received metoclopramide 10 mg i.v. followed by fentanyl 1-2 μg/kg i.v. before induction as premedication. Anesthesia was induced with thiopental 3-5 mg/kg i.v., intubation with succinylcholine 1-2 mg/kg i.v., maintained with nitrous oxide 66 per cent in oxygen and a neuromuscular blocking agent, supplemented with fentanyl and halothane. After intubation, a suction catheter was inserted orally to aspirate the gastric contents and was retained to the end of operation for stomach decompression. No patients received fentanyl during the last 30 minutes of the operation. Residual neuromuscular blocking effect was reversed with i.v. neostigmine 2.5 mg and atropine 1.2 mg. The diagnosis, type of operation, incision line, operation time, and the amount of perioperative fentanyl were recorded.

All variables were assessed in a double-blind fashion for each of the patients. Pain scores were assessed by the patients using the verbal numerical scale (0 = no pain at all to 10 = the worst pain imaginable). A numeric scale was chosen because of the practical difficulties with postoperative patients completing a visual analogue scale, particularly immediately following surgery. The severity of pruritus was assessed in the same manner (0 = no pruritus at all to 10 = the most unbearable pruritus). The severity of nausea was assessed on a scale 0-3 (0 = no nausea, 1 = mild: little nausea, 2 = moderate to severe: much nausea but no treatment needed, 3 = severe: severe nausea which need rescue antiemetics). Sedation was assessed in the postanesthesia care unit (PACU) by one of our investigators and a PACU nurse, and on the ward by a ward nurse and the patient's report using sedation scores on a scale 0-3 (0 = no sedation at all, 1 = mild sedation or drowsy, 2 = moderate sedation or asleep but responsive to verbal or physical stimulus, 3 = oversedation or unarousable).

Upon arrival in the PACU, the Abbott Pain Management Provider (Abbott Laboratories, North Chicago, IL) was attached to an i.v. cannula. The PCA solution, morphine 40 mg with or without droperidol (Janssen Pharmaceutica, Brussels, Belgium) 2.5 mg added into normal saline to 100 ml solution, was prepared for each patient according to Random Number Table by a nurse anesthetist. The investigators were blind to this procedure. The patients were randomly allocated into 2 groups. Group M (n = 48) received morphine alone. Group MD (n = 46) received morphine and droperidol. The patients' vital signs, nausea and vomiting were observed. The time the patients needed antiemetics was recorded. The time to sedation score 0-1 was recorded. With sedation scores 0-1, the patients reported their pain scores at rest and on coughing when they requested analgesics. The amount of morphine for a loading dose was calculated according to their pain scores using the equation[5]:

$$\text{Morphine (mg)} = \{0.053 + (0.004)\ \text{Pain score at rest}\}\ \text{Body weight (kg)}$$

Each patient was then given a half of the calculated amount as a loading dose from the prepared PCA solution *via* a PCA device[5]. The time to first analgesic was recorded and was termed Time 0. The PCA device was set to deliver a bolus dose of morphine 1 mg (group M) or morphine 1 mg and droperidol 0.0625 mg (group MD) with a lockout interval of 5 minutes, a 4-hour limit of 20 mg morphine with no continuous infusion. The patient was reminded to press the button for pain as needed. Having left the PACU, patients were returned to their wards where standard nursing observations were maintained.

At Time 0, then at 2, 6, 18, and 24 hours of using PCA, the patients' vital signs, the amount of morphine and droperidol used, pain scores at rest and on coughing, nausea scores, the episodes of vomiting, the amount of metoclopramide and the time received, sedation scores, pruritus scores, and the presence of nasal congestion and other untoward effects were recorded. The number of times nurses were called to give care for pain, PONV and other side effects on the ward was recorded at hour 6, 18, and 24. At the end of the study, the patients reported their satisfaction score (0 = not satisfied at all to 100 = completely satisfied) for postoperative analgesia provided. The patients' comments and problems were recorded.

Statistical Analysis

The statistical package SPSS for Windows was used. The data were analyzed for presence of normal distribution using the Kolmogorov-Smirnov goodness of fit test. Continuously distributed, parametric variables are expressed as mean ± SD and were analyzed by the Student *t*-test. Nonparametric variables were analyzed by chi-square test, Fisher's exact test, Mann-Whitney test. The University of British Columbia (UBC) Clinical Significance Calculator was used to analyze Absolute Risk Reduction, Relative Risk Reduction and Number Needed to Treat. $p<0.05$ was considered statistically significant.

RESULTS

No significant differences were found between the groups with respect to age, weight, height, body mass index, ASA classification, history of motion sickness or postoperative nausea and vomiting (PONV) after previous anesthesia, incision line, operation time, the amount of fentanyl received perioperatively, time to sedation score 0-1, and time to first analgesic requirement (Table 1).

The incidence of postoperative nausea in both groups before starting PCA was 14.9 per cent (14/94), and vomiting was 4.3 per cent (4/94). During the immediate postoperative period to the first 2 hours of PCA use, group MD had more patients with

Table 1. Demographic data.

	Group M n = 48	Group MD n = 46	P value
Age (yr)	43.5 (6.6)	42.9 (5.7)	0.611
Weight (kg)	57.5 (9.7)	57.3 (9.1)	0.894
Height (cm)	155.2 (5.4)	156.8 (4.9)	0.128
BMI (kg/m^2)	23.9 (3.8)	23.3 (3.9)	0.525
ASA (I : II)	42 : 6	40 : 6	1.000
History of motion sickness (Yes)	3	1	0.606
History of PONV after previous anesthesia (Yes)	6	8	0.635
Incision line (Pfannenstiel : low midline)	29 : 19	29 : 17	0.960
Operation time (min)	119.5 (42.9)	120.5 (44.8)	0.912
Perioperative fentanyl (mcg)	91.5 (24.1)	92.1 (28.6)	0.914
Time to sedation score 0-1 (min)	18.9 (10.2)	21.3 (14.4)	0.461
Time to first postoperative analgesic (min)	31.0 (18.9)	36.1 (40.3)	0.432

Values are number of patients and mean (SD).
M = morphine, MD = morphine and droperidol. PONV = postoperative nausea and vomiting.

nausea and vomiting than group M did, but the differences were not significant (Table 2 and 3). Then the number of patients with nausea and vomiting in group MD began to be lower than in group M throughout 24 hours, with a statistically significant difference for nausea during hour 6-18 and 18-24 (Table 2). The effect of droperidol on the risk of nausea is shown in Table 2. After hour 2, the incidence of vomiting was lower in group MD than in group M, but the difference was not statistically significant (Table 3).

During hour 2-6, 6-18, and 18-24 of PCA use, the number of patients in group MD with nausea scores 2 and 3 was significantly lower than in group M (Table 4).

Group M vomited a total of 85 times during 24 hours of PCA use with 1, 16, 53, and 15 times during hour 0-2, 2-6, 6-18, and 18-24, respectively. Group MD vomited a total of 50 times in 24 hours with 4, 12, 31 and 3 times during hour 0-2, 2-6, 6-18 and 18-24, respectively. However, the differences were not statistically significant (p=0.269).

There were 13 patients (27%) who received metoclopramide as a rescue antiemetic in group M, and 6 patients (13%) in group MD, but this showed no statistical difference (p=0.151). Group M received a total dose of metoclopramide 200 mg with a mean 4.17 (SD 8.21) mg whereas group MD received a total dose of 90 mg or 1.96 (5.82) mg, but this showed no statistical difference (p=0.125).

Table 2. Number of patients with nausea and the effect of droperidol on the risk of nausea.

	Group M n = 48		Group MD n = 46		P value
	N	%	N	%	
After operation, before starting PCA	4	8.3	10	21.7	0.125
0-2 h of PCA use	10	20.8	11	23.9	0.912
2-6 h of PCA use	24	50	15	32.6	0.133
6-18 h of PCA use	29	60.4	17	37	0.039
18-24 h of PCA use	20	41.7	7	15.2	0.013
0-24 h of PCA use	32	66.7	24	52.2	0.222
6-18 h postoperatively					
Absolute Risk Reduction (ARR)	0.23	(95% CI 0.04-0.43)			
Relative Risk Reduction (RRR%)	39	(95% CI 5-60)			
Number Needed to Treat (NNT)	4	(95% CI 2-27)			
18-24 h postoperatively					
Absolute Risk Reduction (ARR)	0.27	(95% CI 0.09-0.44)			
Relative Risk Reduction (RRR%)	64	(95% CI 23-83)			
Number Needed to Treat (NNT)	4	(95% CI 2-11)			

N = number of patients, M = morphine, MD = morphine and droperidol, CI = Confidence Interval.

Table 3. Incidence of vomiting in each time interval.

	Group M n = 48		Group MD n = 46		P value
	N	%	N	%	
After operation, before starting PCA	1	2.1	3	6.5	0.356
0-2 h of PCA use	1	2.1	3	6.5	0.356
2-6 h of PCA use	8	16.7	5	10.9	0.607
6-18 h of PCA use	16	33.3	11	23.9	0.435
18-24 h of PCA use	6	12.5	2	4.4	0.271
0-24 h of PCA use	21	43.8	13	28.3	0.178

N = number of patients, M = morphine, MD = morphine and droperidol.

Table 4. Degree of nausea in each time interval.

	Group M, n = 48 Nausea score (0-3)						Group MD, n = 46 Nausea score (0-3)						P value
	0		1		2 & 3		0		1		2 & 3		
	N	%	N	%	N	%	N	%	N	%	N	%	
After operation, before starting PCA	44	91.7	3	6.2	1	2.1	36	78.3	6	13	4	8.7	0.289
0-2 h of PCA use	38	79.2	8	16.6	2	4.2	35	76.1	6	13	5	10.9	0.429
2-6 h of PCA use	24	50	9	18.8	15	31.2	31	67.4	10	21.7	5	10.9	0.032
6-18 h of PCA use	19	39.6	12	25	17	35.4	29	63.1	10	21.7	7	15.2	0.024
18-24 h of PCA use	28	58.4	10	20.8	10	20.8	37	84.1	5	11.4	2	4.5	0.025

N = number of patients, M = morphine, MD = morphine and droperidol.

Table 5. Amount of morphine received in each time interval.

	Group M mg		Group MD mg		P value
	Mean	SD	Mean	SD	
At 0 h (loading dose)	2.34	0.52	2.22	0.42	0.216
0-2 h of PCA use	5.23	3.4	4.39	3.51	0.240
2-6 h of PCA use	5.17	3.7	4.22	3.46	0.203
6-18 h of PCA use	7.6	4.32	5.63	4.23	0.028
18-24 h of PCA use	4.38	3.38	3.5	2.66	0.174
Total morphine received in 24 h	24.72	9.97	19.81	10.58	0.023
Total morphine received / kg	0.44	0.2	0.35	0.19	0.037

M = morphine, MD = morphine and droperidol.

There were 9 and 8 patients in groups M and MD, respectively, who had a history of motion sickness or previous PONV. One patient in group MD had a history of both. Among those 9 patients in group M, 8 patients (88.9%) had nausea. It occurred before starting PCA in 3 patients (33.3%). Five patients (55.6%) had moderate nausea. Seven patients (77.8%) vomited, with 29 episodes of vomiting. Together, 6 patients (66.7%) received metoclopramide with a total dose of 90 mg. Among those 8 patients in group MD, nausea occurred in 4 patients (50%). One patient (12.5%) had moderate nausea before starting PCA. Two patients (25%) vomited, with 9 episodes of vomiting. Only one patient (12.5%), the one with moderate nausea before starting PCA, needed metoclopramide with a total dose of 30 mg.

The amount of morphine received during hour 6-18 of PCA use in group MD was significantly less than in group M (Table 5) whereas there were no differences between groups in pain scores both at rest and on coughing in each period of time (Table 6 and 7).

Vital signs were normal throughout the 24 hours of the study. No patients were oversedated (Table 8). Pruritus occurred in 7 and 1 patients (14.6% and 2.2%) in groups M and MD, respectively, with no significant difference (p=0.317). Nasal congestion was found in 2 patients, one in each group.

One patient in group MD had an oculogyric crisis and opisthotonos, which were extrapyramidal reactions, after 7 hours of PCA use or 8 hours after premedication with metoclopramide. She was fully conscious and had normal vital signs. At that time, she had received morphine 17.5 mg and droperidol 1.09 mg. The investigator gave her midazolam 2.5 mg i.v.. The symptoms disappeared and she could sleep. Later, in hour 11 after pressing the PCA button, she developed the symptoms again. We then stopped PCA use and gave her diazepam 5 mg i.v., and the symptoms disappeared. She had received morphine 18.5 mg and droperidol 1.16 mg in total. Blood electrolyte and calcium levels were normal. She was then given morphine i.m. for pain instead.

Table 6. Pain score (verbal numerical scale, 0-10) at rest, in each time interval.

	Group M n = 48		Group MD n = 46		P value
	Mean	SD	Mean	SD	
Preoperation	0.4	1.3	0.2	0.5	0.420
After operation, before starting PCA	6.7	2.5	5.8	2.4	0.094
0-2 h of PCA use	5.2	2.1	5.5	2.5	0.563
2-6 h of PCA use	4.0	2.2	4.2	2.5	0.622
6-18 h of PCA use	2.8	2.3	2.7	2.0	0.788
18-24 h of PCA use	2.6	1.9	1.9	1.6	0.062

M = morphine, MD = morphine and droperidol.

Table 7. Pain score (verbal numerical scale, 0-10) on coughing, in each time interval.

	Group M n = 48		Group MD n = 46		P value
	Mean	SD	Mean	SD	
After operation, before starting PCA	7.1	2.5	6.5	2.1	0.209
0-2 h of PCA use	6.3	2.2	7.0	1.9	0.146
2-6 h of PCA use	6.0	2.3	6.2	2.4	0.777
6-18 h of PCA use	5.0	2.2	5.4	2.3	0.354
18-24 h of PCA use	4.7	1.9	4.3	2.0	0.299

M = morphine, MD = morphine and droperidol.

The number of times nurses were called to give care for pain, PONV and other side effects during hour 2-6, 6-18, and 18-24 of PCA use in groups M and MD was 0.8 (1.03), 1.0 (1.44), and 0.37 (0.61); and 0.9 (1.83), 1.27 (2.08), and 0.55 (1.03), respectively. There were no significant differences between each group (p=0.795, 0.564, and 0.407, respectively).

The patients' satisfaction scores for pain relief *via* PCA for 24 hours in groups M and MD were 85.9 (11.6), and 90.8 (10.2), respectively. The difference was statistically significant (p=0.046).

The direct medical cost was calculated from drug and consumable item cost only, including morphine, droperidol, metoclopramide, midazolam, diazepam, syringes and needles. In group M (n = 48), the total amount of morphine used in 24 hours was 1,186.54 mg, of metoclopramide was 200 mg, and 20 sets of syringes and needles were used. These cost US$54.79/group or US$1.14/patient in group M. In group MD (n = 46), the patients used 911.04 mg morphine, 56.45 mg droperidol, 90 mg metoclopramide, 2.5 mg midazolam, 5 mg diazepam, and 11 sets of syringes and needles. The cost was US$ 48.48/group or US$1.05/patient in group MD.

DISCUSSION

Clinical observations indicate that patients often find the side effects of analgesics, particularly nausea and vomiting, more distressing than the postoperative pain for which they are prescribed. When using patient-controlled analgesia (PCA), some patients seem willing to endure pain rather than suffer unpleasant side effects and it has been proposed that patients may in fact balance pain against side effects [12,13]. Postoperative nausea and vomiting (PONV) often limits patients' successful use of PCA. Although some have found differences in incidence and intensity of side effects between agent[13] in relation to PONV, there appears to be no clear advantage to using one opioid over the others. No one opioid stands out as preferential for use in PCA and the extent to which PONV are caused by the opioids that patients are receiving *via* PCA is still not clear. The relationship between opioid use and PONV is complex and warrants further investigation as does the use of antiemetics with PCA[3]. Research into minimizing these unpleasant side effects is imperative.

In this study, droperidol was used because it is not expensive and is a potent antiemetic. Low dose droperidol given during anesthesia has been

Table 8. Degree of sedation in each time interval. No patients had a sedation score = 3.

	Group M, n = 48 Sedation score (0-3)						Group MD, n = 46 Sedation score (0-3)						P value
	0		1		2		0		1		2		
	N	%	N	%	N	%	N	%	N	%	N	%	
After operation, before starting PCA	9	18.8	39	81.2	0	0	11	23.9	32	69.6	3	6.5	0.144
0-2 h of PCA use	9	18.8	29	60.4	10	20.8	11	23.9	29	63.1	6	13	0.620
2-6 h of PCA use	17	35.4	25	52.1	6	12.5	7	15.2	31	67.4	8	17.4	0.066
6-18 h of PCA use	22	45.8	20	41.7	6	12.5	24	52.2	14	30.4	8	17.4	0.530
18-24 h of PCA use	33	68.8	12	25	3	6.2	33	71.7	10	21.8	3	6.5	0.975

N = number of patients, M = morphine, MD = morphine and droperidol.

shown to treat or prevent nausea and vomiting during the early postoperative period. It has been reported that the addition of droperidol 0.016-0.167 mg/1-2 mg morphine in PCA can reduce nausea and vomiting[7-11,14-19], but at a dose of 0.167 mg droperidol/mg morphine, the patients were oversedated[11]. Some investigators commented that the minimum clinically effective amount of droperidol, 0.0625-0.1 mg/mg morphine, should be employed since extrapyramidal reactions can occur.

In this study, we added droperidol at a dose of 0.0625 mg/mg morphine. We found that patients received a mean of 1.26 (SD 0.67) mg in 24 hours or 0.02 (0.01) mg/kg in 24 hours, which reduced the incidence of nausea in hour 6-18 and 18-24 from 60 per cent and 42 per cent to 37 per cent and 15 per cent, respectively. The number needed to treat in both intervals was 4. This implies that of 100 patients treated with droperidol added to PCA morphine, 40 did not suffer nausea but if they had not received droperidol they would have been nauseated. The severity of nausea was also reduced from hour 2 throughout the 24 hours of PCA use. Although the total amount of metoclopramide as a rescue antiemetic was lower in group MD than in group M, the difference was not statistically significant. If we used the amount of rescue antiemetic requirement to calculate a sample size, we need n = 208 to get a power = 0.8.

The investigators had tried to decrease the possibility of nausea and vomiting occurring in the immediate postoperative period, in order to observe PONV clearly, by premedication with metoclopramide and insertion of a suction catheter to decompress stomach. We found that the severity and the incidences of nausea and vomiting before PCA use (14.9% and 4.3%, respectively) were lower, compared with other studies after major gynecological surgery, in which the incidence of PONV was 58-77 per cent[9,20]. If the patients got so much PONV that they needed antiemetics before starting PCA, the study might be affected. As the elimination half-life of metoclopramide is 2-4 hours, the incidence of PONV immediately after surgery up to 2 hours of PCA use was low. We used metoclopramide, which has the same site of action as droperidol but a lower potency and shorter duration, because we wanted the antiemetic effects to last only a short period before starting PCA.

Some investigators have given droperidol as premedication in a dose of 1-2.5 mg i.v., and postoperative analgesia was provided by PCA containing droperidol 0.04-0.1 mg/mg morphine[14-17]. They found that sedation scores were low but were increased with the increasing doses of droperidol mixed with morphine in PCA. Some investigators gave droperidol 0.5-1.25 mg i.v. as a prophylactic dose just before or at the end of surgery followed by a combination of droperidol and morphine. They found that sedation was increased when the PCA dose contained droperidol 0.083-0.167 mg/mg morphine [7,8,10]. However, in the studies that the dose of droperidol in PCA was around 0.016-0.05 mg/mg morphine, there was no increase in sedation[21,22]. Gan, et al.[7] found that droperidol given either as a single dose at the end of surgery or mixed in morphine PCA can reduce the incidence of PONV, but the addition of droperidol in morphine PCA following a single dose of droperidol at the end of surgery should be avoided in view of the greater degree of sedation without further reduction in the incidence of PONV. Nevertheless, Roberts, et al.[8] commented

that sedation did not result in any morbidity because it occurred around 8-12 hours postoperatively which was during a night rest.

The incidences of nausea and vomiting in patients with a history of either motion sickness or PONV after previous anesthesia were not very high after receiving several measures preventing PONV. In this group of patients, the incidence and severity of PONV, the amount of antiemetics needed, and the number of patients who needed it were lower in those who received PCA morphine containing droperidol than in those who received PCA morphine alone.

As there are 4 different types of receptors, there are at least 4 sites of action of the antiemetics. Antiemetic agents may have actions at more than one receptor, but they tend to have a more prominent action at 1 or 2 receptors. Hence, a combination of drugs will probably have greater antiemetic action than a single drug without an increase in side effects[2]. Wrench, et al.[22] suggested that combination therapy may be indicated specifically where a history of PONV is obtained. They showed that a combination of ondansetron (a $5HT_3$ receptor antagonist) and droperidol was significantly more effective than either agent alone for prevention of PONV following gynecological surgery.

In other studies, the amount of morphine needed by the patients was not different between groups[7, 8,14-17,21,22]. In our study, we found that group MD needed less morphine than group M did in hour 6-18 of PCA use but that there was no difference in other periods. The pain scores in both groups were similar. It was possible that during hour 6-18 of PCA use that usually was at night, the patients in group MD might sleep better, so they pressed PCA button less frequently. Consequently, nausea and vomiting occurred less. Whether droperidol enhanced the analgesic effect of morphine, it is still controversial.

Nasal congestion can occur after administration of droperidol. We found this side effect in just a few cases and the symptom was not severe, as no patients had previous history of it. The incidence of pruritus after receiving morphine in group MD was less than in group M, but the difference was not significant. It could be that the sample size was too small to demonstrate it.

The patient in group MD who had an extrapyramidal reaction might be sensitive to droperidol because the amount she had received was very small (within limits of safe use)[19]. However, extrapyramidal reactions have been reported to occur in ASA I adults at 24 hours after a single dose of droperidol 0.65 mg[23]. Approximately 1 per cent of patients receiving droperidol exhibit extrapyramidal muscle movements, which are sometimes delayed for 12 hours after termination of anesthesia[24]. Merridew and Keefe[25] reported that, in their series of over 400 patients having subcutaneous infusion of morphine and droperidol (1-2.5 mg per 24 hours), extrapyramidal reactions occurred in about 1 per cent. The patient in our study developed her first symptoms after receiving droperidol 1.1 mg in 7 hours, and further symptoms at 12 hours of PCA use with a total dose of 1.16 mg droperidol before PCA was stopped.

The patient received droperidol close to metoclopramide (about 1 hour after) but this might not be the cause of the extrapyramidal reaction. To our knowledge, there have never been any reports of the enhancement of side effects after simultaneous administration of these two drugs, though they are both dopamine (D_2) antagonists.

Another side effect of droperidol that has been described is akathisia. Akathisia literally means an inability to sit still. It is characterized by a sense of restlessness that is often uncomfortable or unpleasant. Foster, et al.[26] found that 30.7 per cent of their patients given droperidol 0.5 and 1 mg developed this side effect, and suggested that it might be dose related. No patients in our study reported this side effect.

Although the satisfaction score of pain relief reported by the patients was statistically different between groups, clinically it was not different. Those with high satisfaction scores commented that the PCA method was easy to use, convenient, no need to call for nurse when they were in pain, and could relieve pain quickly. Most of the patients with lower satisfaction scores complained a lot about nausea and vomiting.

Cost-effective analysis done by Watcha and Smith[27] showed that prophylactic antiemetic therapy was cost-effective for operations with a high frequency of emesis, whereas treatment of established symptoms was more cost-effective when the frequency was lower. When drug costs, efficacy, and adverse events were all considered, prophylactic droperidol was more cost-effective than ondansetron and metoclopramide. In this study, as the number of times nurses were called to give care for pain,

PONV and other side effects was not different, we calculated only the drug and consumable item cost. We found that addition of droperidol to PCA morphine did not increase the cost whereas it could reduce the incidence and severity of nausea.

The authors have demonstrated that the addition of droperidol to morphine PCA is very useful and should be used in patients who have histories that suggest a high possibility of PONV or after operations with a high frequency of emesis. Droperidol can be given at a low dose (1-1.25 mg i.v.) as a premedication, then added to morphine PCA in a low dose, to avoid sedation and extrapyramidal reactions. If it is found that nausea and vomiting cannot be prevented, we can then adjust the dose of droperidol to 0.05-0.08 mg/mg morphine to control the symptoms adequately.

SUMMARY

In conclusion, we have demonstrated that the addition of droperidol 0.0625 mg/mg morphine for postoperative analgesia with PCA method, significantly prevented and reduced postoperative nausea in patients underwent gynecological operation. With the dose we used, vomiting and the amount of antiemetics needed could be reduced but the differences were not statistically significant. The groups had similar pain scores. No patients were oversedated. The drug and consumable item cost was not different between groups. An extrapyramidal reaction developed in one patient.

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การใช้ยาโดรเพอริดอลร่วมกับมอร์ฟินโดยวิธี patient–controlled analgesia†

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ผู้วิจัยได้ทำการศึกษาประสิทธิผลและผลข้างเคียงของการใช้โดรเพอริดอลร่วมกับมอร์ฟินที่บริหารโดยใช้เครื่อง patient–controlled analgesia (PCA) โดยศึกษาในผู้ป่วย 94 รายที่มารับการผ่าตัดเอามดลูกออกทางหน้าท้องหลังจากได้รับการระงับความรู้สึกตามมาตรฐาน แบ่งผู้ป่วยเป็น 2 กลุ่มโดยวิธีสุ่ม กลุ่มควบคุมได้รับมอร์ฟินทางเครื่อง PCA เมื่อกดปุ่มปล่อยยาแต่ละครั้ง 1 มก. กลุ่มศึกษาได้รับมอร์ฟิน 1 มก. และโดรเพอริดอล 0.0625 มก. ในแต่ละครั้ง โดยมีระยะเวลา lockout 5 นาที และไม่มีการหยดยาเข้าอย่างต่อเนื่องเช่นเดียวกัน พบว่าอุบัติการณ์และความรุนแรงของอาการคลื่นไส้ในกลุ่มที่ได้รับมอร์ฟินและโดรเพอริดอลต่ำกว่ากลุ่มที่ได้รับมอร์ฟินเพียงอย่างเดียว แต่จำนวนครั้งของการอาเจียนไม่แตกต่างกัน ไม่มีผู้ป่วยที่ง่วงซึมผิดปกติ แต่มี 1 รายในกลุ่มที่ได้รับมอร์ฟินและโดรเพอริดอลเกิดปฏิกิริยา extrapyramidal ซึ่งอาการหายไปได้เมื่อหยุดยา โดยสรุปการให้โดรเพอริดอลร่วมกับมอร์ฟินทาง PCA สามารถลดอาการคลื่นไส้ แต่ยาในขนาดที่ใช้ไม่สามารถลดอาการอาเจียนได้

คำสำคัญ : PCA, โดรเพอริดอล, มอร์ฟิน, ระงับปวดหลังผ่าตัด, คลื่นไส้, อาเจียน

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