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Prophylactic antiemetic therapy with droperidol in patients undergoing laparoscopic cholecystectomy

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Abstract
Purpose. The incidence of postoperative nausea and vomiting (PONV) following laparoscopic cholecystectomy (LC) is relatively high when no prophylactic antiemetic is given. We have studied the efficacy of a commonly used and well-established antiemetic, droperidol, for the prevention of PONV in patients undergoing LC.
Methods. In a randomized, double-blind, placebo-controlled study, 60 patients received placebo (saline) or droperidol 50 μg·kg^{-1} (maximum dose, 2.5 mg) intravenously immediately before the induction of anesthesia (n = 30 of each). A standard general anesthetic technique was employed throughout.
Results. A complete response, defined as no PONV and no need for another rescue antiemetic medication during the first 24 h after anesthesia, was 57% and 83% in patients who had received placebo and droperidol 50 μg·kg^{-1}, respectively ($P < 0.05$). No clinically serious adverse events were observed in any of the groups.
Conclusion. Prophylactic antiemetic therapy with droperidol 50 μg·kg^{-1} (maximum dose, 2.5 mg) is highly effective for preventing PONV after LC.

Key words: Laparoscopic cholecystectomy, Nausea, Vomiting, Droperidol

Introduction

Postoperative nausea and vomiting (PONV) are common and unpleasant complications after surgery performed under general anesthesia [1]. The reported incidence of PONV in patients undergoing laparoscopic cholecystectomy (LC) is 25%–42% when no prophylactic antiemetic is provided [2,3]. Ondansetron and granisetron, recently introduced serotonin (5-HT$_3$) antagonists, are effective in preventing PONV after gynecological surgery [4,5], and are also effective in reducing the incidence of PONV after LC [6,7]. We recently compared the efficacy and safety of granisetron, which is more potent and has longer-acting activity than ondansetron [8], with droperidol for the control of PONV in patients undergoing LC [9]. Consequently, granisetron 3 mg (approximately 60 μg·kg^{-1}) is more effective than droperidol 1.25 mg (approximately 25 μg·kg^{-1}) in reducing the incidence and severity of PONV in this population [9]. However, granisetron (¥10 200 for 3 mg) as well as ondansetron (¥10 300 for 3 mg) is much more expensive than droperidol (¥175 for 2.5 mg), which is widely used for preventing PONV [10–13]. Two different doses of droperidol, 1.25 mg and 2.5 mg, reduce the incidence of PONV following gynecological or orthopedic surgery [10,12]. Although this antiemetic is used widely, there are no studies available on its efficacy for preventing PONV in patients undergoing LC. We have recently demonstrated that prophylactic therapy with droperidol 1.25 mg (approximately 25 μg·kg^{-1}) is ineffective for the control of PONV after LC [9]. Therefore, this study was designed to assess the antiemetic efficacy of droperidol 50 μg·kg^{-1} (maximum dose, 2.5 mg) for preventing PONV in patients undergoing LC.

Materials and methods

After institutional review board approval and informed consent, we studied 60 patients, 45 females and 15 males [American Society of Anesthesiologists (ASA) physical status I–II], aged 24–63 years, undergoing LC. Patients who had gastrointestinal diseases, those who were pregnant or menstruating, and those who had taken an antiemetic medication within 24 h before surgery were excluded from the study.

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Patients received no preanesthetic medication. Patients received, in a randomized, double-blind manner, a single dose of placebo (saline) or droperidol 50 μg·kg^{-1} (maximum dose, 2.5 mg) i.v. immediately before the induction of anesthesia. Anesthesia was induced with thiopentone 5 mg·kg^{-1} i.v., and vecuronium 0.2 mg·kg^{-1} i.v. was used to facilitate tracheal intubation. After tracheal intubation, anesthesia was maintained with nitrous oxide (N_2O) 66% and isoflurane 1.0%–3.0% (inspired concentration) in oxygen. Ventilation was controlled mechanically and was adjusted to keep $P_{ET}CO_2$ at 35–40 mmHg throughout the surgery using an anesthetic/respiratory analyzer (Ultima, Datex, Helsinki, Finland). A nasogastric tube was inserted and suction applied to empty the stomach of air and other contents. Muscle relaxants were used as required. During laparoscopy, intraabdominal pressure was maintained automatically at 10 mmHg by a CO_2 insufflator. At the end of surgery, reversal of muscle relaxation was achieved with atropine 0.02 mg·kg^{-1} i.v. and neostigmine 0.04 mg·kg^{-1} i.v., and then tracheas were extubated. After tracheal extubation, the nasogastric tube was again suctioned and then removed. Rectal temperature was monitored and maintained at 37 ± 1°C during surgery. If two or more episodes of PONV occurred during the first 24 h after anesthesia, another rescue antiemetic (e.g., metoclopramide 10 mg i.v.) was given. Postoperatively, patients received indomethacin 50 mg rectally as required when they complained of pain.

Postoperatively, all episodes of PONV (nausea, retching, vomiting) experienced by the patients were recorded every 3 h within the first 24-h postoperative period by direct questioning by nursing staff who had no knowledge of which drugs (placebo or droperidol) the patients had received, or by spontaneous complaint by the patients. Nausea was defined as the subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as the labored, spasmic, rhythmic contraction of the respiratory muscles without the expulsion of gastric contents; vomiting was defined as the forceful expulsion of gastric contents from the mouth [1]. A complete response was also defined as no PONV and no need for another rescue antiemetic medication during the first 24 h after anesthesia. The details of any adverse effect throughout the study were also recorded by follow-up nurses who interviewed the patients, or by spontaneous complaints of patients.

Statistical analysis was performed with ANOVA with Bonferroni's correction for multiple comparison, χ^2 test, or Fisher's exact probability test, as appropriate. A P value of < 0.05 was considered significant. All values were expressed as mean ± SD or numbers (%).

Results

Demographic data were not significantly different among the groups (Table 1).

A complete response was greater in patients who had received droperidol 50 μg·kg^{-1} (83%) than in those who had received placebo (57%) ($P < 0.05$) (Table 2).

The most frequently reported adverse effects were headache, dizziness, and drowsiness, which were not serious. There were no differences in the incidence of these symptoms between the groups (Table 3). Excessive sedation and extrapyramidal symptoms were not observed in any of the groups.

Table 1. Patient characteristics

	Placebo (n = 30)	Droperidol (n = 30)
Age (years)	47 ± 9	47 ± 11
Sex (female/male)	23/7	22/8
Height (cm)	158 ± 7	156 ± 6
Weight (kg)	56 ± 7	55 ± 8
History of motion sickness (n)	4	5
History of previous PONV (n)	3	3
Duration of operation (min)	85 ± 36	85 ± 31
Duration of anesthesia (min)	109 ± 37	109 ± 32
Indomethacin administered postoperatively (n)	22	21

Values are mean ± SD or numbers.

Table 2. Numbers and % (in parentheses) of patients having a complete response (no PONV, no rescue), and nausea, retching, vomiting, or requiring another rescue antiemetic during the first 24 h after anesthesia

	Placebo (n = 30)	Droperidol (n = 30)	P
Complete response (no PONV, no rescue)	17(57)	25(83)	0.024
Nausea	5(17)	3(10)	0.353
Retching	1(3)	0(0)	0.5
Vomiting	7(23)	2(7)	0.073
Rescue	7(23)	2(7)	0.073

Values are numbers (with % in parentheses).

Table 3. Incidence of adverse effects

	Placebo (n = 30)	Droperidol (n = 30)
Headache	2	2
Dizziness	1	1
Drowsiness	2	2
Others (constipation, muscle pain)	1	2

Discussion

Postoperative nausea and vomiting (PONV) are among the most frequent complications after anesthesia and surgery, with a relatively high incidence following LC [2,3]. The etiology of PONV is complex and is dependent on a variety of factors, including patient demographics, types of surgery, anesthetic technique, and postoperative care [1]. The main patient-related factors are age, sex, obesity, and history of motion sickness and/or previous PONV. Surgical factors also include the effect of intraperitoneal CO_2 insufflated on residual stretching and irritation of the peritoneum [3]. Preanesthetic medication (e.g., atropine, hydroxyzine) has been reported to decrease the incidence of PONV [1]. Postoperative analgesia using opioids is associated with the occurrence of emetic symptoms [1]. In this study, however, the treatment groups were similar for patient demographics, surgical procedure, anesthetics administered, and analgesic (indomethacin) used postoperatively, and preanes-thetic medication was not performed. Therefore, the difference in a complete response (no PONV, no rescue) between the groups can be attributed to the difference in the agent administered.

The use of N_2O during laparoscopy has been considered to be an important problem because of concerns regarding its ability to produce bowel distension during the surgery and to increase the incidence of PONV [14]. Taylor et al. [15] have recently studied the efficacy and safety of N_2O specifically during general anesthesia for LC, and have found no differences between the groups receiving air and these receiving N_2O with respect to operating conditions, bowel distention, or the incidence of PONV. In this study, therefore, we used N_2O as an adjuvant anesthetic in patients undergoing LC.

The incidence of PONV (i.e., no complete response) in this study was relatively high (43%) without an administration of prophylactic antiemetic medication. This incidence was consistent with previous reports about the incidence of PONV after LC, which ranged from 25% to 42% [2,3].

Droperidol, a dopamine receptor antagonist, has been shown to be effective for preventing PONV [10–13]. We have found no study evaluating its efficacy for the control of PONV in patients undergoing LC. In this study, we demonstrated that a complete response (no PONV, no rescue) within the first 24-h postoperative period was greater in patients who had received droperidol $50\,\mu g \cdot kg^{-1}$ (83%) than in those who had received placebo (57%) ($P < 0.05$). This suggests that droperidol $50\,\mu g \cdot kg^{-1}$ is effective for preventing PONV after LC.

We found a remarkably high incidence of a complete response (83%) during the first 24 h after anesthesia for LC in patients who had received droperidol $50\,\mu g \cdot kg^{-1}$. This incidence was almost comparable to our previous report that an emesis-free episode occurred in 89% of patients who had received granisetron [9]. Thus, if droperidol was used to prevent PONV after LC, antiemetic medication costs would be reduced.

The adverse effects observed in this study were not serious, and there were no differences in the incidence of headache, dizziness, and drowsiness between the groups. Excessive sedation and extrapyramidal symptoms were not observed in any of the groups. Thus, droperidol $50\,\mu g \cdot kg^{-1}$ (maximum dose, 2.5 mg) is considered to be safe for the prevention of PONV in patients undergoing LC. However, when used in larger doses (more than 2.5 mg), serious side effects may occur in this population [1].

In conclusion, prophylactic antiemetic therapy with droperidol $50\,\mu g \cdot kg^{-1}$ (maximum dose, 2.5 mg) is highly effective for preventing PONV in patients undergoing LC.

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