

Post-Laparoscopic Vomiting in Females versus Males: Comparison of Prophylactic Antiemetic Action of Ondansetron versus Metoclopramide

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ABSTRACT

Background and Objectives: The incidence of postoperative vomiting in patients undergoing laparoscopic cholecystectomy is compared in females versus males. The report also compares the prophylactic action of ondansetron versus metoclopramide.

Methods: A total of 85 American Society of Anesthesiologists (ASA) I and II patients were enrolled in the study. Patients were divided into two groups according to sex: Group I 53 females, and Group II 32 males. After anaesthetic induction, subjects received intravenously either 4 mg ondansetron or 10 mg metoclopramide.

Results: The incidence of vomiting as well as the frequency of emetic episodes over 24 hours were analyzed in each group using X2 analysis. Data analysis revealed a significantly higher incidence ($P < 0.05$) of postoperative emesis in females 10:53 (18.9%) as compared to males 0:32 (0%). In the male group, no patient vomited postoperatively, whether prophylactic ondansetron or metoclopramide was used. While the incidence of emesis in the female group was lower ($P < 0.05$) in the ondansetron group (17.6%) than the metoclopramide group (29.6%).

Conclusion: These results may indicate prophylactic antiemetic therapy in female patients undergoing laparoscopic cholecystectomy; ondansetron appears to be superior to metoclopramide.

Key Words: Laparoscopic cholecystectomy, Vomiting, Sex, Ondansetron, Metoclopramide.

INTRODUCTION

Postoperative nausea and vomiting (PONV) has been called the "Big Little Problem."¹ It can often be the main cause of prolonged hospital stay. Recent studies have shown the general incidence of postoperative emesis to be in the 20-30% range,²⁻⁶ while the incidence of post-laparoscopic vomiting is 35%.^{7,8} Previous investigators have reported a significantly higher incidence of vomiting after non-laparoscopic surgery in females as compared to male adults, including postmenopausal females until the age of 70 years,^{2,3,5,9} suggesting a hormonal pharmacologic basis for the susceptibility of females to vomiting. Drugs used in the prevention of postoperative vomiting include anti-histaminics, anticholinergics, dopamine receptor antagonists, and 5HT₃ antagonists. The purpose of this study is to compare in patients undergoing laparoscopic cholecystectomy the incidence of vomiting in females versus males, and to compare the prophylactic antiemetic action of ondansetron (a selective 5HT₃ antagonist) versus metoclopramide (a dopamine receptor antagonist).

METHODS

The study was approved by our hospital research committee. Approved consent was taken from the patients preoperatively. American Society of Anesthesiologists (ASA) Class I and II patients scheduled for laparoscopic cholecystectomy were chosen. A total of 85 patients were enrolled in the study. The following data were collected on all patients: age, weight, history of diabetes, motion sickness, previous postoperative nausea or vomiting, as well as days since the last menstrual period (LMP) in females. Also, anaesthetic techniques, duration of surgery, and postoperative analgesia were recorded. The patients were then divided into two groups according to sex. Group I consisted of 53 females, and Group II consisted of 32 males. A random number was used to assign prospectively each patient to receive after induction of anesthesia either ondansetron 4 mg (A), or metoclopramide 10 mg (B). The staff caring for these patients were blinded to the study drug received.

All patients were premedicated with meperidine 75 mg, atropine 0.6 mg and promethazine 25 mg intramuscularly

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Table 1.
Demographic Data.

Characteristics	FEMALE		MALE	
	Ondansetron (A)	Metoclopramide (B)	Ondansetron (A)	Metoclopramide (B)
Age (yrs)	48.3 ± 16.6	41.3 ± 13.4	47.1 ± 12.7	43.5 ± 9.8
Weight (kg)	68.3 ± 10.7	69.1 ± 11.6	87.5 ± 18.0	84.3 ± 18.8
History of Motion sickness	2	2	0	1
History of Diabetes	1	1	2	
Number of days since LMP	2-45 (16 ± 14)	1-30 (13.2 ± 9.3)	-	-
PREVIOUS ANAESTHESIA				
None	10	10	5	8
Without nausea & vomiting	15	14	12	5
With nausea & vomiting	1	3	1	1
Duration of surgery (min.)	102.6 ± 22.9	90.9 ± 28.7	103.3 ± 17.8	115.8 ± 28.9
Need for analgesics	11	11	9	7
TOTAL	26	27	18	14

45 minutes prior to the induction of anesthesia. After standard monitoring (EKG, noninvasive blood pressure and oximetry) was applied, all patients were induced with thiopentone 5 mg/kg, fentanyl 2 µg/kg and vecuronium 0.1 mg/kg. Following induction of anesthesia, patients received randomly either ondansetron 4 mg (A) or metoclopramide 10 mg (B). Anesthesia was maintained by N₂O:O₂ mixture (2:1) and supplementary doses of vecuronium. All patients had a nasogastric tube inserted intraoperatively that was removed at the end of surgery. The duration of operation was recorded and neuromuscular blockade was reversed by a mixture of neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. In the recovery room, an independent blinded observer recorded emetic episodes, vital signs, oxygen saturation and pain scores for two hours postoperatively. Drugs administered, such as narcotics or antiemetics, were also recorded.

After two hours, patients were discharged to the floor, where they were followed up to 24 hours by another independent observer; the number of patients who vomited was recorded in each group. The degree of pain and medications administered were also recorded. The incidence of emetic episodes over 24 hours were analyzed in each group, using X² analysis at 95% confidence interval. P<0.05 was considered significant.

RESULTS

Laparoscopic cholecystectomy during the study period was more frequent in females than in males.

There were no differences between study groups with respect to age, anaesthetic technique, duration of operation, diabetes, days since the last menstrual period in females, or history of previous postoperative nausea and vomiting as well as the need for postoperative analgesics (**Table 1**).

All recorded episodes of vomiting were associated with the forceful expulsion of gastric contents; none of the data represents an episode of retching. As shown in **Table 2**, the incidence of emesis was significantly higher in the female group than in the male group (P<0.05). In the male group, no patient vomited postoperatively, whether

Table 2.
Incidence of Vomiting.

	Total Number	Vomiting	No Vomiting
Females	53	10	43
Males	32	0	32

	Total Number	Vomiting	No Vomiting
Ondansetron (A)	26	2	24
Metoclopramide (B)	27	8	19

prophylactic ondansetron or metoclopramide was used. In the female group, the incidence of postoperative emesis was significantly lower ($P < 0.05$) in the ondansetron group than the metoclopramide group (**Table 3**).

DISCUSSION

The present study shows in patients undergoing laparoscopic cholecystectomy that females have a significantly higher incidence of postoperative vomiting than males. This finding confirms the gender difference that exists between adult males and females below the age of 70 years, that was published many years ago by Bellville² in patients undergoing non-laparoscopic surgery under general anesthesia. Variations in serum gonadotropin (or other hormonal) levels may be a factor in the higher incidence of postoperative vomiting in females. Gonadotropin level is known to rise at menopause for several years before falling, which coincides with the age of 70 years when the gonadotropin level falls. At this age, the incidence of vomiting in females approaches that seen in males.² In males, our report shows that the incidence and severity of vomiting is low, whether metoclopramide or ondansetron is used as a prophylactic antiemetic. However, in females, where there is a higher incidence of vomiting, prophylactic administration of ondansetron appears to be superior to metoclopramide.

The low incidence of vomiting in the present study, as compared to previous studies, may be attributed to the fact that we considered only patients who vomited, and did not include nausea, which can be subjective. Also, our patients were premedicated with promethazine and atropine. Atropine premedication has been shown to decrease the incidence of vomiting,¹⁰ and promethazine (an antihistaminic with both antidopaminergic and antimuscarinic action) has been also shown to decrease the incidence of postoperative vomiting.⁵

Postoperative vomiting is multifactorial in origin; both the type of anesthesia and surgery, duration of surgery, along with postoperative pain or analgesic (narcotics) contribute to its etiology. The mechanisms can be either central or peripheral.^{9,11} There are four major neurotransmitters which play a role in mediating the emetic response: dopaminergic, histaminergic (H1), cholinergic muscarinic and 5HT₃.^{9,11} Therefore, drugs used for the prevention of postoperative vomiting are usually antihistaminics, anticholinergics, and dopamine receptor antagonists.^{12,13} However, these drugs possess clinically significant untoward side-effects (sedation, dry mouth, dysphoria and extrapyramidal symptoms) which often may limit their use, especially in ambulatory surgery.

Ondansetron, a selective antagonist of 5HT₃ receptors, has been effectively used for the prevention of chemotherapy-induced emesis. Chemotherapy-induced emesis is secondary to the release 5HT₃ from the shedding of the mucosa of the gut during chemotherapy.¹⁴ Also, ondansetron has been shown in many recent studies to be effective for the prevention of nausea and vomiting in high risk operations such as laparoscopic surgery,¹⁵ post-strabismus repair in children¹⁶ and gynecologic surgery,¹⁷ with little side effects.^{18,19} Metoclopramide, on the other hand, blocks dopamine receptors at the chemoreceptor trigger zone (CTZ); also, it increases lower esophageal sphincter tone and enhances gastric and small bowel motility.⁹ However, metoclopramide failed to reduce the incidence of PONV after major gynecologic surgery^{12,13} and laparoscopic surgery.²⁰ The short duration of action of metoclopramide may explain its lack of efficacy in preventing PONV.

The present report has shown that prophylactic ondansetron is superior to metoclopramide in patients undergoing laparoscopic cholecystectomy. Intra-abdominal operations are more associated with postoperative vomiting than extra-abdominal operations. Manipulations and traction on the gut during abdominal surgery discharge vagal and splanchnic afferents to the central nervous system.¹¹ In addition to this mechanism, surgical manipulation of the intestine also induces release of 5HT₃ from the enterochromaffin cells.¹¹ That is why ondansetron, a selective 5HT₃ antagonist, can be the antiemetic of choice following intra-abdominal surgery.

In conclusion, the incidence of post-laparoscopic cholecystectomy vomiting is significantly higher in females than in males. Because of the high incidence of vomiting in

females, prophylactic antiemetic therapy may be indicated. Ondansetron prophylaxis appears to be superior to metoclopramide.

References:

1. Kapur PA. The big little problem. *Anesth Analg*. 1991;73:243-245.
2. Bellville JW, Bross IDJ, Howland WS. Postoperative nausea and vomiting IV: factors related to postoperative nausea and vomiting. *Anesthesiology*. 1960;21:186-193.
3. Beattie WS, Lindbad T, Buckley DN, Forrest JB. The incidence of post-operative nausea and vomiting in women undergoing laparoscopy is influenced by the day of the menstrual cycle. *Can J Anaesth*. 1991;38:298-302.
4. Forrest JB, Cahalan MK, Rehder K, et al. Multicenter study of general anesthesia: II. Results. *Anesthesiology*. 1990;72:262-268.
5. Burtles P, Pecket BW. Postoperative vomiting. Some factors affecting its incidence. *Br J Anaesth*. 1964;29:114-153.
6. Bellville JW. Postanesthetic nausea and vomiting. *Anesthesiology*. 1961;22:773-780.
7. Patasky AV, Kitz DS, Andrews RW, Leckry JH. Nausea and vomiting following ambulatory surgery. *Anesth Analg*. 1988;67(suppl):163.
8. Metter SE, Kitz PS, Young MC, et al. Nausea and vomiting after outpatient laparoscopy, incidence, impact on recovery room stay and cost. *Anesth Analg*. 1987;66:S116.
9. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology treatment and prevention. *Anesthesiology*. 1992;77:162-184.
10. Dundee JW, Nicholl RM, Moore J. Studies of drugs given before anaesthesia. A method for the studying of their effects on postoperative vomiting and nausea. *Br J Anaesth*. 1962;34:527-535.
11. Andrews PLF. Physiology of nausea and vomiting. *Br J Anaesth*. 1992;69(suppl):25-195.
12. Madej TH, Simpson KH. Comparison of the use of domperidone, droperidol and metoclopramide in the prevention of nausea and vomiting following major gynaecological surgery. *Br J Anaesth*. 1986;58:884-887.
13. De Silva PHDP, Darvish AH, Mac Donald SM, Cronin MK, Clark K. The efficacy of prophylactic ondansetron, droperidol, perphenazine, and metoclopramide in the prevention of nausea and vomiting after major gynecologic surgery. *Anesth Analg*. 1995;81:139-143.
14. Hawthorn D, Ostler J, Andrews PLR. The role of the abdominal visceral innervation and 5HT M receptors in vomiting induced by the cytotoxic drugs cyclophosphamide and cisplatin in the Ferret. *Quarterly J Experimental Physiology*. 1988;73:7-21.
15. Sung YF, Wetchler BV, Bancely D, Josly AF. A double blind placebo controlled pilot study examining the effectiveness of intravenous ondansetron in the prevention of postoperative nausea and emesis. *J Clin Anesth*. 1993;5:72-79.
16. Brose J, Martin TM, Coddry DH, et al. Ondansetron reduces the incidence and severity of poststrabismus repair vomiting in children. *Anesth Analg*. 1994;79:476-479.
17. Mchenzie R, Kovac A, O'Conner T, Duncalf D, Angel J, et al. Comparison of ondansetron versus placebo to prevent postoperative nausea and vomiting in women undergoing ambulatory gynecologic surgery. *Anesthesiology*. 1993;78:21-28.
18. Leeser J, Lip H. Prevention of postoperative nausea and vomiting using ondansetron, a new selective 5HT₃ receptor antagonist. *Anesth Analg*. 1991;72:751-755.
19. Khalil SN, Kararia B, Pearson K, et al. Ondansetron prevents postoperative nausea and vomiting in women outpatients. *Anesth Analg*. 1994;89:845-851.
20. Raphael JH, Norton AC. Anti-emetic efficacy of prophylactic ondansetron in laparoscopic surgery: randomized double blind comparison with metoclopramide. *Br J Anaesth*. 1993;71:845-848.