Journal of Anesthesia & Clinical Research
ISSN: 2155-6148

Farhat et al., J Anesthe Clinic Res 2013, 4:3
DOI: 10.4172/2155-6148.1000297

Research Article Open Access

Comparison of Ondansetron and Metoclopramide for PONV Prophylaxis in Laparoscopic Cholecystectomy

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Abstract

Background: Postoperative nausea and vomiting (PONV) are common distressing complications of surgery and anaesthesia.

Objective: The present study was designed to compare the relative antiemetic efficacy and safety of intravenous (I/V) ondansetron and metoclopramide for prevention of PONV after elective laparoscopic cholecystectomy in adult female patients under General Anesthesia (GA).

Material and methods: In this prospective, randomized, placebo-controlled, double-blind study we included 150 adult American Society of Anesthesiologists (ASA) Grade I or II female patients, aged 18-55 years, undergoing elective laparoscopic cholecystectomy under GA. The anaesthetic technique, drugs, monitoring and care were standardized in all the patients during the perioperative period. The patients were divided into two groups using random numbers table. Group A (n=50) received ondansetron 4 mg/2ml while group B (n=50) received metoclopramide 10 mg/2 ml I/V just before induction of anaesthesia. Patients were observed for the initial 24 hours after anesthesia. The presence or absence of nausea and vomiting (by simply yes or no) was assessed by a resident anesthetist double blind to the study The rescue antiemetic (cyclizine 10 mg) I/V, was given, if patient suffered from nausea for more than 15 minutes, or experience retching or vomiting during study period.

Results: In comparison to metoclopramide group, the frequency of nausea and vomiting was clinically and statistically lower in ordansetron group (p=0.035). Use of rescue antiemetic was significantly higher in metoclopramide group (p=0.022).

Conclusion: Our study showed that prophylactic use of ondansetron is more effective with fewer side effects than metoclopramide in the prevention of PONV during laparoscopic cholecystectomy in adult females. Furthermore, metoclopramide was associated with more adverse effects, major being dizziness and extrapyramidal symptoms.

Keywords: PONV; GA; Laparoscopy; Ondansetron; Metoclopramide; Cholecystectomy

Introduction

Postoperative Nausea And Vomiting (PONV) are common distressing complications of surgery and anaesthesia [1,2]. Along with pain, this is often listed by the patient as their most important perioperative concerns [3]. It also leads to increased costs related to length of hospital stay. Laparoscopic surgeries are associated with an appreciably high rate of PONV [2] because of the creation of pneumoperitonium during the procedure [4]. Despite the use of modern anesthetic practices, the incidence of this condition still remains to be around 80% in high risk groups [5]. It is believed that PONV is multifactorial. Among the many factors, female gender, past history of PONV and motion sickness, use of opioids, nitrous oxide and non-smoking history are the independent predictors for PONV [6]. It may lead to serious surgical complications such as wound dehiscence or surgical site bleeding, resulting in delay in prolong hospital stays, burdening the country's economy [7]. The incidence of PONV can be as high as 80% in the high-risk patients underlying the importance of its prevention and control by anesthetists [8].

So far several drugs have been used for preventing PONV. Most of them act as antagonist at the receptors which are involved in emesis. The traditional anti emetics include antihistamines, anticholinergics and dopamine-receptor antagonists [9]. Early ambulation and reduced morbidity are the advantages of the drug therapy. However, they have limited efficacy in PONV and are associated with side effects such as sedation and extra pyramidal signs [10]. Newer class of drugs, such as the Serotonin Receptor Antagonists (SRA) provides better efficacy and safety as compared to the traditional drugs. Ondansetron, a prototype of this group is widely used drug of this group in our country [1,3,10]. It binds to the 5-Hydroxytryptamine subtype 3 (5HT3) receptors, selectively blocking the emetogenic stimuli during anesthesia and surgery. The drug has a proven efficacy and is recommended as a prophylactic antiemetic at the time of induction of anesthesia [11].

Metoclopramide is a Dopamine (D2) receptor antagonist. It has antiemetic properties and is widely used for the prevention and treatment of PONV. Its untoward effects include extrapyramidal reactions (oculogyric crisis, opisthotonus, trismus, torticollis), abdominal cramping, sedation, dizziness and cardiac dysrhythmias . Tachycardia, weakness, subcutaneous emphysema, epistaxis, hypotension, eye disturbances, pruritis, itching, delirium emergens, dry mouth and taste or smell disturbances are some of the other side effects that have been reported [7,9,12]. This study was aimed at determining the efficacy and

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Received January 28, 2013; **Accepted** March 14, 2013; **Published** March 18, 2013

Citation: Farhat K, Pasha AK, Kazi WA (2013) Comparison of Ondansetron and Metoclopramide for PONV Prophylaxis in Laparoscopic Cholecystectomy. J Anesthe Clinic Res 4: 297. doi:10.4172/2155-6148.1000297

safety of single dose of ondansetron and metoclopramide in preventing PONV in females undergoing elective laproscopic cholecystectomy.

Material and Methods

The study protocol was approved by the Ethical Committee of Centre for Research in Experimental and Applied Medicine (CREAM), Army Medical College, Rawalpindi, Pakistan. The study was conducted in the Operation Theatre (OT), Combined Military Hospital, Rawalpindi from January to June 2012. A written/informed consent was obtained from all the patients.

Study design

This was a prospective, randomized, placebo-controlled, double-blind study.

Inclusion criteria: We included 150 adult ASA I or II female patients, aged 18-55 years, undergoing elective laparoscopic cholecystectomy.

Exclusion criteria: Patients with ASA grade III and IV, BMI>30 kg/m^2, history of motion sickness, upper gastrointestinal pathology like acid peptic disease, reflux esophagitis, pyloric stenosis, hiatus hernia, history of substance abuse, patients taking anti-emetic, anti-psychotic or chemotherapeautic drugs 24 hours before surgery, known allergy to the drugs included in the study, any history of nausea, retching or vomiting within past 24 hours, cardiovascular, central nervous system, haematologic, renal or hepatic disease, menstruating or pregnant patients and length of surgery more than 90 minutes were excluded from the study.

The patients were admitted the day before surgery. Pre-anaesthesia assessment was carried out by a Consultant Anaesthetist who was blind to the study. The necessary investigations were carried out and any co-morbid conditions were excluded. Patients were kept nil by mouth for 6-8 hours. No opiod analgesic was given preoperatively. On arrival in the OT, an 18 gauge I/V cannula was passed in the non-dominant hand. Perioperative monitoring included pulse-oximetry, non-invasive blood pressure every 3 min, temperature, capnography and continuous ECG. Ringer Lactate solution was given as a fluid therapy during the perioperative period.

All the drugs for the study were prepared by a fully-trained anaesthesia nurse who was not involved in the study; in identical syringes (colors of the drugs were also identical). A randomization list and sealed envelopes were prepared before anesthesia according to a list of randomized numbers generated. This exercise was followed to ensure that the anesthesiologist, patients, and PACU nurses remained blinded to the identity of the prophylactic treatment. Patients were premedicated with injection midazolam 0.04 mg/kg body weight and injection Tramadol 2 mg/kg body weight and preoxygenated with 100% oxygen for 5 min. They were divided into three groups using random numbers table.

Group A (n=50) received ondansetron 4 mg while group B (n=50) received metoclopramide 10 mg diluted in 5 ml distill water ml I/V slowly just before the induction of anaesthesia. In all the patients, midazolam 0.04 mg/kg I/V was used for pre-medication. 100% oxygen was given through anaesthesia mask. Induction of anaesthesia was carried out with freshly prepared solution of injection thiopental 5 mg/kg body weight I/V slowly followed by atracurium 0.4 mg/kg for muscle relaxation and adequate size endotracheal tube was passed. Anaesthesia was maintained with 60% N_2O in oxygen using Bain-Circuit. Incremental standard dose of atracurium was repeated, if required intra-operatively.

At the cessation of surgical procedure, anaesthetic drugs were discontinued and neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg I/V and 100% oxygen was started. Endotracheal tube was removed after gentle suctioning of oropharyngeal secretions. Surgical wounds were infiltrated with 0.125% bupivicaine in 10 ml solution and ketorolac 30 mg I/V was given as postoperative analgesia. Oxygen was continued till the patient was fully awake and obeying commands. The patients were then shifted to the Post-anesthesia Care Unit (PACU), where they were evaluated by a Resident Anesthetist who was double-blinded to the study.

For the initial 24 hours post-anaesthesia, the presence or absence of nausea and vomiting (simply by yes or no) was assessed by anesthetist. Nausea was defined as the subjectively unpleasant sensation associated with awareness of the urge to vomit, whereas vomiting was defined as the forceful expulsion of gastric contents from the mouth. Any side-effects of the drugs were also recorded. The rescue antiemetic (cyclizine 10 mg), I/V were given, if patient remained nauseous for more than 15 minutes, or experienced retching or vomiting.

Statistical analyses were performed using SPSS (Statistical Package for Social Sciences) version 17. Qualitative variables were expressed as percentage while quantitative variables were expressed as mean ± SD (standard deviation). We used Student t-test for analyzing age, weight, duration of surgery and duration of anesthesia while chi-square test was utilized for the gender, ASA physical status, and frequency of nausea and vomiting and use of rescue antiemetic. P-value less than 0.05 were considered statistically significant.

Results

All the 100 patients, 50 in each group were included in the study. There were no significant differences between the two groups with regard to regards to age (p=0.276), weight (p=0.562), height (0.153), ASA physical status (0.624), BMI (0.643) and), duration of surgery (p=0.740), and duration of anesthesia (p=0.804) as shown in Table 1.

The frequency of nausea and vomiting was lower in the ordansetron group as compared to the metoclopramide group and the results were statistically significant (p=0.032; Figure 1). In group A, 88.6% patients did not have nausea or vomiting postoperatively, while 11.4% experienced nausea. In group B, 42.4% had nausea, 7.8% had vomiting, while 57.6% of patents did not complain of either nausea or vomiting (Table 2 and Figure 2). Use of rescue antiemetic shown in Figure 3, was significantly higher in metoclopromide group (p=0.022). None of the patients experienced headache, flushing or other side effects.

Discussion

Nausea and vomiting are protective reflexes against the absorption of toxins, as well as responses to certain stimuli. PONV is amongst the

Variables Mean ± SD	Group A n=50	Group B n=50	P-Value (<0.05)
Age(y) ± SD	42.4 ± 7.8	40.8 ± 8.2	p=0.276*NS
Weight(kg) ± SD	66.8 ± 4.8	68.2 ± 5.4	p=0.562*NS
Height (in)	49.4 ± 14.6	49.4 ± 14.6	p=0.153*NS
BMI kg/m^2	49.4 ± 14.6	49.4 ± 14.6	p=0.643*NS
ASA (I/II)	42/8	44/6	p=0.624*NS
Duration of surgery (min)	62.4 ± 7.8	60.8 ± 8.2	p=0.740*NS
Duration of anaesthesia (min)	86.8 ± 6.4	87.4 ± 5.8	p=0.804*NS

Values are expressed as mean ± SD; * Significance (p<0.05)

Table 1: Patient demographic data and operative characteristics.

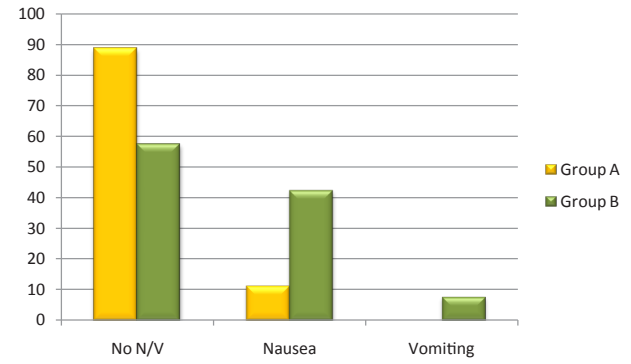

Figure 1: Nausea and vomiting in group A and group B.

Study Groups	Headache	Dizziness	Sedation	Any Other
Group A	1 (2%)	2 (4%)*	1 (2%)*	0 (0%)
Group B	5 (10%)	8 (16%)	7 (14%)	2 (4%)

Values are expressed as percentage (%); *Significance ($p<0.05$)

Table 2: Incidence of adverse effects.

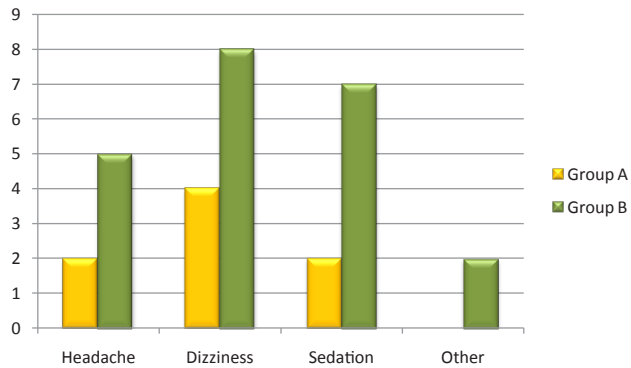

Figure 2: Adverse effects in group A and group B.

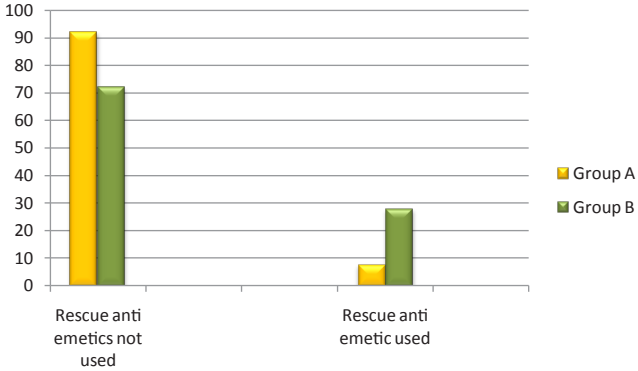

Figure 3: Requirement of rescue anti emetic in group A and group B.

most common complications following anesthesia and surgery with a selectively high incidence (upto 70%) after laparoscopic cholecystectomy [2,7]. The etiology of PONV after laparoscopic cholecystectomy is multifactorial. There are multiple causes of PONV like pharyngeal stimulation, gastrointestinal distention, abdominal surgery, anesthetic agent, pain, opioids, hypoxia, hypotension, vestibular disturbances and psychological factors. Certain factors can pre-dispose patient to PONV, like age (more in children), gender (female), history of previous nausea and vomiting, history of motion sickness, long-duration surgeries and anesthesia, carbon dioxide retention, type of surgical procedure [2].

In our study, we kept a number of variables constant for both the study groups. We included only female gender, all patients received laparoscopic cholecystectomy, and anesthesia was induced by the same team of anesthetists. Anesthetic drugs and technique were standardized, including postoperative analgesics. Duration of anesthesia and surgery was comparable and there was no difference in age, gender, weight, BMI of patients in both groups. Moreover, we also excluded patients with a previous history of motion sickness or PONV. Our aim was to ensure that the difference in the incidence of PONV among the groups can be attributed to the difference in drugs tested for their efficacy in preventing PONV. We selected metoclopramide to compare against ordansetron since the former is one of the most commonly used antiemetic agent [13].

For qualitative comparison between the groups in our study, we compared two drugs, metoclopromide and ordansetron with each other. This study showed that ordansetron 4 mg as compared with metoclopramide 10 mg administered in female adult patients undergoing elective laparoscopic cholecystectomy under GA significantly decreases the frequency of PONV (Figure 1). Prior studies reported a variable incidence of PONV after using ordansetron as a prophylaxis. Our conclusions were in agreement with Fujii [9], Karen B et al.[14], Helmy [15], Enrico[16], Ali [17], Ambreen [18], Diemunsch [19,20], However, Enrico and associates used diazepam for premedication which can itself lead to emesis. Diemunsch et al. though studied the two drugs in the treatment of established PONV. We must mention here that it was not possible to determine whether ordansetrom monotherapy had an antiemetic effect since we did not include a placebo group. Nevertheless, a complete response (no nausea/vomiting) was observed in 86.4% of patients in ordansetron group in our investigation. In contrary to our study deductions, Richard et al. found out that metoclopramide is more effective in preventing PONV than ordansetron [21] but they combined metoclopramide with droperidol. Conversely, Daria and Kumar found out that metoclopramide has not only a low (36.7%) success rate in the prevention of PONV, but it has also a higher incidence of side effects. They also observed a lesser success rate in the prevention of PONV is poor in Ondansetron group as well [3]. Additional published studies support our deductions where a similar reduction in the incidence of PONV was observed during 24 hour post recovery period [22-25].

Conclusion

Our study showed that prophylactic use of ondansetron is more effective with fewer side effects than metoclopramide in the prevention of PONV during laparoscopic cholecystectomy in adult females. Furthermore, metoclopramide was associated with more adverse effects, major being dizziness and extrapyramidal symptoms.

References

1. Park SK, Cho EJ (2011) A Randomized, Double-Blind Trial of Palonosetron Compared with Ondansetron in Preventing Postoperative Nausea and Vomiting after Gynaecological Laparoscopic Surgery. The Journal of International Medical Research 39: 399-407.

2. Ahmed Nisar, Muslim M, Aurangzeb M, Zarin M (2012) Prevention of postoperative nausea and vomiting in laparoscopic cholecystectomy. J Med Sci 20: 33-36.

3. Daria U, Kumar V (2012) Qualitative comaparison of metoclopramide, ordansetron and granisetron alone and in combination with dexamethasone in

the prevention of postoperative nausea and vomiting in day care laparoscopic surgery under general anaesthesia. Asian J Pharm Clin Res 5: 165-167.

4. Gecaj-Gashi A, Hashimi M, Sada F, Baftiu N, Salihu S, et al. (2010) Propofol vs isoflurane anesthesia-incidence of PONV in patients at maxillofacial surgery. Adv Med Sci 55: 308-312.
5. Srivastava A, Niranjan A (2010) Secrets of safe laparoscopic surgery: Anaesthetic and surgical considerations. J Minim Access Surg 6: 91-94.
6. Chandrakantan A, Glass PS (2011) Multimodal therapies for postoperative nausea and vomiting, and pain. Br J Anaesth 107: i27-i40.
7. Aziz N, Naz U, Ilyas M (2011) A comparative study between metoclopramide and dexamethasone for prevention of postoperative nausea and vomiting in laparoscopic cholecystectomy. J Med Sci 19: 129-132.
8. Apfel CC, Laara E, Koivuranta M, Greim CA, Roewer N (1999) A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. Anesthesiology 91: 693-700.
9. Fujii Y (2008) Clinical strategies for preventing postoperative nausea and vomitting after middle ear surgery in adult patients. Curr Drug Saf 3: 230-239.
10. Pawar AN, Sarkar M, Dewoolkar L (2009) Comparative study of single dose intravenous dexamethasone, ondansetron and ondansetron plus dexamethasone as prophylactic anti-emetic therapy in patients undergoing laparascopic gynaecological surgery. The Internet Journal of Anesthesiology 19: 135.
11. Shams TMA, Nahla E, Raga EI (2012) Prophylactic small doses of mixture of 5-HT3 receptor antagonists and dexamethasone on PONV and adverse effects. EJICT 1: 132-138.
12. Rumore MM (2012) Cardiovascular adverse effects of metoclopramide: Review of literature. IJCRI 3: 1-10.
13. Ismail S (2008) Practice of use of antiemetic in patients for laparoscopic gynaecological surgery and its impact on the early (1st two hrs) postoperative period. J Pak Med Assoc 58: 203-205.
14. Domino KB, Anderson EA, Polissar NL, Posner KL (1999) Comparative efficacy and safety of ondansetron, droperidol, and metoclopramide for preventing postoperative nausea and vomiting: a meta-analysis. Anesth Analg 88: 1370-1379.
15. Helmy SA (1999) Prophylactic anti-emetic efficacy of ondansetron in laparoscopic cholecystectomy under total intravenous anaesthesia. A randomised, double-blind comparison with droperidol, metoclopramide and placebo. Anaesthesia 54: 266-271.
16. Polati E, Verlato G, Finco G, Mosaner W, Grosso S, et al. (1997) Ondansetron versus metoclopramide in the treatment of postoperative nausea and vomiting. Anesth Analg 85: 395-399.
17. Ali AH (2008) Comparison of Drugs and Intravenous Crystalloid in Reduction of Postoperative Nausea and Vomiting after Laparoscopic Surgery. World Journal of Laparoscopic Surgery 1: 29-34.
18. Khan A, Iqbal M, Yunus A, Ali K (2011) Comparison of ondansetron and metoclopramide in the prevention of post-operative nausea and vomiting after laparoscopic cholecystectomy.
19. Diemunsch P, Conseiller C, Clyti N, Mamet JP (1997) Ondansetron compared with metoclopramide in the treatment of established postoperative nausea and vomiting. The French Ondansetron Study Group. Br J Anaesth 79: 322-326.
20. Krobbuaban B, Pitakpol S, Diregpoke S (2008) Ondansetron vs. metoclopramide for the prevention of nausea and vomiting after gynecologic surgery. J Med Assoc Thai 91: 669-674.
21. Steinbrook RA, Freiberger D, Gosnell JL, Brooks DC (1996) Prophylactic antiemetics for laparoscopic cholecystectomy: ondansetron versus droperidol plus metoclopramide. Anesth Analg 83: 1081-1083.
22. Hill RP, Lubarsky DA, Phillips-Bute B, Fortney JT, Creed MR, et al. (2000) Cost-effectiveness of prophylactic antiemetic therapy with ondansetron, droperidol, or placebo. Anesthesiology 92: 958-967.
23. Figueredo E (2000) Ondansetron and evidence-based medicine. Anesth Analg 91: 496-497.
24. Grimsehl K, Whiteside JB, Mackenzie N (2002) Comparison of cyclizine and ondansetron for the prevention of postoperative nausea and vomiting in laparoscopic day-case gynaecological surgery. Anaesthesia 57: 61-65.
25. Olutoye O, Jantzen EC, Alexis R, Rajchert D, Schreiner MS, et al. (2003) A comparison of the costs and efficacy of ondansetron and dolasetron in the prophylaxis of postoperative vomiting in pediatric patients undergoing ambulatory surgery. Anesth Analg 97: 390-396.