ORIGINAL ARTICLE

EFFICACY OF ONDANSETRON AND METOCLOPRAMIDE AGAINST POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Objectives: Comparing the clinical efficacy of the antiemetics (Ondansetron and Metoclopramide) in preventing post-operative nausea and vomiting (PONV) in patients undergoing Laparoscopic Cholecystectomy (LC).

Material and Methods: This is a randomised study conducted at anesthesiology department, Khyber Teaching Hospital, Peshawar, Pakistan from April 2015 to December 2015. Two treatment arms Group A (Ondansetron) and B (Metoclopramide) were created. A sample of 60 patients was selected in each treatment group.

Results: The overall mean age was 43.42 ± 10.8 years with 37 (30.8%) males and 83 (69.2%) females in a ratio of 1 to 2.24. Overall mean weight was 77.08 ± 9.05 Kg. Mean age in group A was 43.5 ± 10.8 years while it was 43.2 ± 10.9 years. Similarly, mean weight in group A was 76.5 ± 9.3 Kg while it was 77.6 ± 8.8 Kg. A Chi-squared test performed for treatment group versus the incidence of PONV showed that PONV in group A was 13.3% while in group B it was 27.5% of the total episodes of PONV with a significant association of PONV with group B ($p = 0.002$). The early PONV episodes occurred in significantly higher proportion in group B as compared to group A (15% group B versus 6.7% in group A, $p = 0.027$). However, late PONV episodes were not significant for any treatment group (6.7% in group A versus 13.3% in group B, $p = 0.068$).

Conclusion: Peri-induction use of intravenous ondansetron is an effective alternative than intravenous metoclopramide in prevention of nausea/vomiting after LC.

Key Words: Nausea, vomiting, laparoscopic cholecystectomy, Ondansetron, Metoclopramide.

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INTRODUCTION

Incidence of nausea and vomiting after laparoscopic cholecystectomy (LC) is high. These symptoms bear negative impact on patient satisfaction and may prolong hospital stay and pharmacologic requirements. The diseases of gall bladder are common in many parts of the world. Globally, cholelithiasis or gall-stones affect an estimated 10-15% of the adults and is more common in women[1]. LC has become the gold standard surgical treatment for gall-stones which is increasingly performed electively. LC is increasingly being performed globally and the total cases of gallbladder removal has surged more than 20% over the previous two decades[2]. The primary reason may be increased experience with learning LC and increased availability of diagnostic and surgical equipment all over the world. Advantages of LC are rapid recovery, shorter stay in the hospital and shorter time to resumption of daily activities.[3]

One of the most common down side of the laparoscopic cholecystectomy is a relatively higher incidence of PONV which is estimated to occur in about 53-70% of postoperative patients. The mechanism cited are many, including accumulation of gas with pressure on the Vagus nerve which may stimulate the brain vomiting centre. Other than this, stimulation in the pharynx,

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gastric distention, anaesthetic agents, severe pain, use of opioid analgesics, very early ambulation and psychological factors[4]. Persistent and refractory PONV can cause dehydration, imbalances of the electrolytes and acid base, aspiration of gastric contents and disruption of the wound.[5,6]

Factors responsible for PONV after LC are positive history of PONV in previous surgeries, patients who experience motion sickness commonly, female gender and younger age[7]. Other contributing factors are obesity, prolonged preoperative fasting, recent food intake, longer anaesthesia duration and depth, CO2 retention, rough handling, type of surgery and number of visitations after surgery.[8,9]

Despite the tremendous advancements in surgical and anaesthetic techniques, one out of three patients still experience PONV and it affects patient satisfaction because recovery from surgery is closely related to patient satisfaction and lower levels of distress[10]. The commonest anti-emetics are 5HT3 antagonists which include Ondansetron and Granisetron[11]. Other antiemetics are anti-cholinergics, dopamine receptor antagonists and antihistamines with significant side effects. Metoclopramide is a well-known antiemetic, which is commonly used in PONV.[12] Our objective in this paper was to compare the efficacy of these commonly used antiemetics, namely metoclopramide and ondansetron in a randomised manner. It will help and strengthen the evidence base and identify the agent most beneficial for PONV.

MATERIAL AND METHODS

This was a prospective randomised non-blind study from the Anaesthesiology department at Khyber Teaching Hospital, Peshawar, Pakistan from April 2015 to December 2015. Two treatment arms were created, Group A for Ondansetron and Group B for Metoclopramide. Sample size for each group was 60 patients. All patients undergoing laparoscopic cholecystectomy for gallstones between age 20 to 65 years irrespective of their gender and good American Society of Anaesthesiologist (ASA) class (I & II) were included. Patients with a history of intake of anti-emetics or emetogenic drugs during the previous 24 hours were excluded. Similarly, uremic patients (BUN > 65 mg/dL), BMI > 29 and diabetic patients were also excluded from the study.

Informed consent was received from all patients at inclusion. After complete history, detailed physical examination and relevant anaesthesia fitness examination, random assignment was done by lottery method. Group A patients received intravenous 4 mg of ondansetron and group B patients received 10 mg metoclopramide at the time of induction of anaesthesia.

For induction of anaesthesia propofol (2 mg/kg) was used while atracurium bromide (0.5 mg/kg). Intravenous ketorolac (30 mg) was used as analgesic. All the laparoscopic cholecystectomies were conducted by the same consultant laparoscopic surgeon. All patients were closely monitored every 30 minutes to determine the efficacy of the drug in the form of PONV. Patient demographics, clinical parameters such as weight, height, comorbids, operation time and the occurrence of PONV was noted.

Data analysis was done with SPSS version 22.0. Quantitative variables were represented using mean ± standard deviations. Chi-square test was performed to determine any association with peri-operative factors. Mann-Whitney U test was used to determine group differences. P-values of <0.05 were considered significant. Efficacy was stratified among age, gender and duration of surgery to see the effect modifiers.

RESULTS

The overall mean age was 43.42 ± 10.8 years with 37 (30.8%) males and 83 (69.2%) females in a ratio of 1 to 2.24. Overall mean weight was 77.08 ± 9.05 Kg. Mean age in group A was 43.5 ± 10.8 years while it was 43.2 ± 10.9 years. Similarly, mean weight in group A was 76.5 ± 9.3 Kg while it was 77.6 ± 8.8 Kg.

Overall 49 (40.8%) patients reported PONV, where 26 (53.09%) reported early PONV (with first 4 hours) while the remaining 24 (48.9%) of PONV occurred during the latter 20 hours (4-24 hours). In group A, 16 (26.7%) patients reported PONV where 8 (13.3%) were during the initial 4 hours postop and the remaining 8 (13.3%) episodes occurred during the latter 20 hours after surgery. In group B, 33 (55.0%) patients reported PONV where 18 (30.0%) episodes occurred in first 4 hours after surgery while the remaining 16 (26.7%) episodes were observed in 4-24-hour period after surgery.

The most common drug side effect note for the entire study population was headache which was noted in 10 (8.3%) patients. This was followed in frequency by dizziness (9, 7.5%), tachycardia and palpitations (8, 6.7%) and hypotension (6, 5.0%).

A Chi-squared test performed for treatment group versus the incidence of PONV showed that PONV in group A was 13.3% while in group B it was 27.5% of the total episodes of PONV with a significant association of PONV with group B ($p = 0.002$). Early PONV episodes occurred in higher proportion in group B than group A (15% group B versus 6.7% in group A, $p = 0.027$). However, late PONV episodes were not significant for any treatment group (6.7% in group A versus 13.3% in group B, $p = 0.068$).

A Mann-Whitney U test was performed for between group differences in terms of PONV and drug side effects. Distribution of PONV for group A and B were not similar as assessed by visual inspection. Significant between group difference was noted for incidence of PONV as well as side effects. Statistics of the Mann-Whitney U test as shown in Table 1.

Table 1: Statistics of the Mann-Whitney U test

	Tx Group	n	Mean Rank	Sum of Rank	Z score	P value
PONV	Ondansetron	60	69.00	4140.00	-3.14	0.002
	Metoclopramide	60	52.00	3120.00		
Early	Ondansetron	60	65.50	3930.00	-2.21	0.027
	Metoclopramide	60	55.50	3330.00		
Late	Ondansetron	60	64.50	3870.00	-1.82	0.069
	Metoclopramide	60	56.50	3390.00		
Headache	Ondansetron	60	61.50	3690.00	-0.66	0.511
	Metoclopramide	60	59.50	3570.00		
Hypotension	Ondansetron	60	63.50	3810.00	-2.50	0.012
	Metoclopramide	60	57.50	3450.00		
Dizziness	Ondansetron	60	64.00	3840.00	-2.42	0.016
	Metoclopramide	60	57.00	3420.00		
Tachycardia	Ondansetron	60	64.50	3870.00	-2.91	0.004
	Metoclopramide	60	56.50	3390.00		

DISCUSSION

LC is currently the gold standard procedure for symptomatic gallstones. Its advantages include less invasive procedure, smaller scar, decreased postoperative pain, less postoperative pulmonary complications, reduced incidence of postoperative ileus, short hospital stay and early mobilisation. The disadvantages include hemorrhage due to injury to major blood vessels, injury to the abdominal viscera, bile leak and injury to the common bile duct (CBD) and PONV. Incidence of PONV is reported to be in the range of 53-70% and it significantly affect patient satisfaction.[13,14]

In this study, we controlled for the confounding factors especially age, obesity, higher ASA class, and postoperative pain. Similar anaesthetic agents were used in all patients with identical pneumoperitoneum pressure. Confounding effects of age and gender were reduced using matched pairs in terms of age and gender groups. Polati et al[15] and Rusthoven et al[9] have adopted similar approach in their studies where they matched age and gender groups for the two treatment arms. Similarly, the above-mentioned studies have shown similar age and gender composition for the study groups.

In our study, group A, 51% patients were operated in 60-120 minutes, 36% patients were operated in 46-60 minutes, and 13% in 30-45 minutes. In group B, 53% patients were operated within 60-120 minutes, 32% in 46-60 minutes, and 15% in 30-45 minutes. The study by Cox F et al[16] has shown similar results in Ondansetron group where 38% patients were operated in 46-60 minutes, and 16% patients were operated in 30-45 minutes. Similarly, the other same study has reported that 58% patients were operated in 60-120 minutes and 14% in 30-45 minutes for the Metoclopramide group.[17]

The incidence of PONV in our study is similar to the one reported by studies of Rusthoven et al[9], and Polati et al[15]. In a meta-analysis, Helmers JH[18] has shown that four milligrams of Ondansetron is clearly beneficial as compared to metoclopramide in alleviating PONV and patients treated with 4 mg dose of Ondansetron consequently respond with higher satisfaction scores. Diemunsch et al[17] in a trial comparing metoclopramide with Ondansetron has shown that the latter is more effective in complete control of PONV, though others have stated that it may control nausea but not vomiting within the first 24 hours after surgery. On the other hand, Helmers[18] and associates have shown that more effective control of PONV can be achieved by using higher doses of Ondansetron. They used 8 mg of ondansetron at the time of induction and noted a significant reduction of PONV (0.001). Khalil and co-workers[19] have shown even a higher efficacy with the combination of ondansetron and promethazine with a reduction to below 30% in the combination arm. Al-Ansari et al[20] in a double-blinded trial has shown that metoclopramide and ondansetron are equally effective for PONV and either can be used to achieve a significant reduction in these symptoms ($p = 0.14$).

CONCLUSION

Ondansetron is favoured because of its safety and tolerability and higher efficacy. The use of ondansetron at the time of induction is recommended.

LIMITATIONS

The limitations of our study are its smaller sample size and single centre experience. Large, multicentre double blinded studies are required to answer the conflicting questions raised by several small trials.

REFERENCES

1. Ebrahim Soltani AR, Mohammadinasab H, Goudarzi M, Arbabi S, Mohammadinasab A, Mohammadinasab F, et al. Comparing the efficacy of prophylactic p6 acupressure, ondansetron, metoclopramide and placebo in the prevention of vomiting and nausea after strabismus surgery. Acta Med Iran. 2011;49(4):208-12.
2. Kaki AM, Abd El-Hakeem EE. Prophylaxis of postoperative nausea and vomiting with ondansetron, metoclopramide, or placebo in total intravenous anesthesia patients undergoing laparoscopic cholecystectomy. Saudi Med J. 2008;29(10):1408-13.
3. Tricco AC, Soobiah C, Blondal E, Veroniki AA, Khan PA, Vafaei A, et al. Comparative safety of serotonin (5-HT3) receptor antagonists in patients undergoing surgery: a systematic review and network meta-analysis. BMC Med. 2015;13:142-47.
4. Wilson EB, Bass CS, Abrameit W, Roberson R, Smith RW. Metoclopramide versus ondansetron in prophylaxis of nausea and vomiting for laparoscopic cholecystectomy. Am J Surg. 2001;181(2):138-41.
5. Reichmann JP, Kirkbride MS. Reviewing the evidence for using continuous subcutaneous metoclopramide and ondansetron to treat nausea & vomiting during pregnancy. Manag Care. 2012;21(5):44-47.
6. Watcha MF, White PF. Post-operative nausea and vomiting: do they matter? Eur J Anaesthesiol Suppl. 1995;10:18-23.
7. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology. 1992;77(1):162-84.
8. Sun R, Klein KW, White PF. The effect of timing of ondansetron administration in outpatients undergoing otolaryngologic surgery. Anesth Analg. 1997;84(2):331-36.
9. Rusthoven J, Obrien B, Rocchi A. Ondansetron versus metoclopramide in the prevention of chemotherapy-induced nausea and vomiting - a metaanalysis. Int J Oncol. 1992;1(4):443-50.
10. Plosker GL, Milne RJ. Ondansetron: a pharmacoeconomic and quality-of-life evaluation of its antiemetic activity in patients receiving cancer chemotherapy. PharmacoEconomics. 1992;2(4):285-304.
11. Morino R, Ozaki M, Nagata O, Yokota M. Incidence of and risk factors for postoperative nausea and vomiting at a Japanese Cancer Center: first large-scale study in Japan. J Anesth. 2013;27(1):18-24.
12. Markham A, Sorkin EM. Ondansetron. An update of its therapeutic use in chemotherapy-induced and postoperative nausea and vomiting. Drugs. 1993;45(6):931-52.
13. Banerjee D, Das A, Majumdar S, Mandal RD, Dutta S, Mukherjee A, et al. PONV in Ambulatory surgery: A comparison between Ramosetron and Ondansetron: a prospective, double-blinded, and randomized controlled study. Saudi J Anaesth. 2014;8(1):25-29.
14. Camu F, Lauwers MH, Verbessem D. Incidence and aetiology of postoperative nausea and vomiting. Eur J Anaesthesiol Suppl. 1992;6:25-31.
15. Polati E, Verlato G, Finco G, Mosaner W, Grosso S, Gottin L, et al. Ondansetron versus metoclopramide in the treatment of postoperative nausea and vomiting. Anesth Analg. 1997;85(2):395-99.
16. Cox F. Systematic review of ondansetron for the prevention and treatment of postoperative nausea and vomiting in adults. Br J Theatre Nurs. 1999;9(12):556-63.
17. Diemunsch P, Conseiller C, Clyti N, Mamet JP. Ondansetron compared with metoclopramide in the treatment of established postoperative nausea and vomiting. The French Ondansetron Study Group. Br J Anaesth. 1997;79(3):322-26.
18. Helmers JH, Briggs L, Abrahamsson J, Soni J, Moodley J, Forrler M, et al. A single i.v. dose of ondansetron 8 mg prior to induction of anaesthesia reduces postoperative nausea and vomiting in gynaecological patients. Can J Anaesth. 1993;40(12):1155-61.
19. Khalil S, Philbrook L, Rabb M, Wells L, Aves T, Villanueva G, et al. Ondansetron/promethazine combination or promethazine alone reduces nausea and vomiting after middle ear surgery. J Clin Anesth. 1999;11(7):596-600.
20. Al-Ansari K, Alomary S, Abdulateef H, Alshawagfa M, Kamal K. Metoclopramide versus ondansetron for the treatment of vomiting in children with acute gastroenteritis. J Pediatr Gastroenterol Nutr. 2011;53(2):156-60.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Ilyas M: Planning of study, manuscript writing
Halimi NN: Data Analysis
Waheed R: Statistic
Salim S: Data management

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.