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Comparison of oral olanzapine versus oral ondansetron for prevention of postoperative nausea and vomiting in female patients undergoing laparoscopic cholecystectomy under general anaesthesia

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Abstract

Introduction: Postoperative nausea and vomiting is one of the significant problem in anaesthesia practice The incidence is even high following laparoscopic surgeries. $5HT_3$ receptor antagonists are routinely used to prevent postoperative nausea and vomiting (PONV). Olanzapine, an atypical antipsychotic drug with its activity on multiple receptor sites particularly at D_2 and $5HT_3$ receptors, has potential antiemetic properties. This study aimed to compare the efficacy of ondansetron with olanzapine in prevention of PONV following laparoscopic cholesystectomy under general anaesthesia.

Materials and methods: This randomized double blind controlled study was done by recruiting 120 female patients belonging to ASA I/II posted for laparoscopic cholecystectomy under general anaesthesia. Patients were assigned to one of the two groups. Group A received tablet Olanzapine 5mg, 4 hrs before surgery and Group B received tablet ondansetron 16mg 1hr before surgery. Postoperatively nausea, retching, vomiting complete response and sedation were assessed for 24hrs at the interval of 0-4hrs, 4-8hrs, 8-12hrs and 12-24hrs.

Results: There was no statistical difference in the incidence of postoperative nausea, retching and vomiting between the groups at 0-4hrs, 4-8hrs. Statistical difference between the groups were seen at 8-12hr interval (nausea p=0.048, retching=0.042, vomiting p=0.042) and at 12-24 hr (nausea p=0.028, retching p=0.001, vomiting p=0.006). There was a significant difference in the use of rescue drug at 8-12hrs (6.7% patients required rescue drug in Group B whereas none required in Group B).

Conclusion: Olanzapine 5 mg can be used safely and effectively for prophylaxis against PONV and is more effective in preventing PONV during the late postoperative period compared to ondansetron.

Keywords: laparoscopic; cholecystectomy; ondansetron; olanzapine; general anesthesia

Introduction

Nausea and vomiting in the postoperative period is one of the most common and distressing symptoms to patients. The general incidence of vomiting is about 30%, nausea is about 50%, and in a subset of high-risk patients, the postoperative nausea and vomiting (PONV) rate can be as high as 70% during the 24hrs after emergence [1]. Although, PONV is rarely fatal, it can result in serious complications such as aspiration pneumonitis, dehydration and disruption of surgical sutures. If not treated may lead to prolonged stay in the post anesthesia care unit, delay in the discharge from the hospital that result in decreased patient satisfaction

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and a significant increase in overall healthcare cost. PONV is multi factorial in origin. Factors which affect the incidence of PONV includes younger age, female sex, history of previous PONV or motion sickness, smoking, intra operative and postoperative opioids surgical procedures like laparoscopic surgeries, breast surgeries, ophthalmic surgeries, ENT surgeries, dental surgeries, duration of surgical procedure and anxiety [2]. Laparoscopic surgeries which are done very commonly now a days has many advantages compared to open surgeries in terms of less surgical trauma, less pain and early discharge. But post-operative nausea and vomiting can be distressing in them.

A number of pharmacological agents have been tried in preventing post-operative nausea and vomiting. Ondansetron, a pro typical drug of 5HT3 antagonist, since its introduction in the early 1990s has been widely used as an antiemetic in patients in PONV and also in chemotherapy induced emesis [3]. Olanzapine, an atypical antipsychotic agent of thiobenzodiazepine class, blocks multiple neurotransmitter receptors including dopaminergic (D_1, D_2, D_3, D_4), serotonergic (5-HT_2A, 5- HT_2C, 5-HT_3, 5-HT_6), adrenergic (alpha1), histaminic (H_1) and muscarinic (m_1,m_2,m_3,m_4) receptor. Because of its action on number of receptors site, it has an advantage over combination of various antiemetics by improving compliance and reducing drug interactions [4]. It is used in chemotherapy induced emesis in cancer patients.

Hence a prospective, randomized, double blind study was done to compare the effect of oral olanzapine with oral ondansetron for preventing PONV in female patients undergoing laparoscopic cholecystectomy surgery under general anesthesia.

The aim of the study was to compare the efficacy of preoperative ondansetron with olanzapine in prevention of postoperative nausea and vomiting following laparoscopic cholecystectomy under general anesthesia.

Materials and methods

This study was a randomized, prospective, double blind study and conducted over a 6 month period from February 2023 to July 2023 at HIMS teaching hospital, Hassan. The study protocol was approved by the institutional ethical committee and informed written consent was taken from patients.

The study population of 120 female patients of age between 18-60 years belonging to either ASA I or ASA II were randomly assigned to one of the two groups using a computer generated random number list. Pre anaesthetic review was done a day before surgery. Group A: Patient received tablet olanzapine 5mg (2 tablets of Olanzapine 2.5mg) 4hrs before surgery with sips of water. Group B: Patients received tablet ondansetron 16mg (2 tablets of ondansetron 8mg) one hour before surgery with sips of water. Monitoring included electrocardiography, oxygen saturation, non invasive blood pressure, end tidal carbon di oxide, respiratory rate (RR). Patients who had pre existing history of esophageal reflux, had history of motion sickness and /or PONV, patients who received opioids or drugs with known antiemetic properties in the last 24hrs were excluded from the study. On arrival to the operating room, an 18G intravenous (I.V) cannula was inserted and an infusion of ringer lactate was started. All the patients were premedicated with inj midazolam 0.03mg/kg, inj glycopyrrolate 0.005mg/kg and inj fentanyl 2mcg/kg. Preoxygenated with 100% O_2 for five minutes, induced with inj thiopentone 5mg/kg. Muscle relaxation achieved with inj vecuronium 0.1mg/kg, intubated with appropriate size endotracheal tube. Once the endotracheal tube was secured an oro gastric tube was introduced and suctioning was done to empty the stomach from air and other contents.

Anaesthesia was maintained with Oxygen 33%. Nitrous oxide 66%, isoflurane 1-2% and inj vecuronium 0.02mg/kg. Inj paracetamol 1gm iv. was given intraoperatively. At the end of surgery patient were reversed with neostigmine 0.05mg/kg and glycopyrrolate 0.01mg/kg. The oro gastric tube was suctioned and then removed before tracheal extubation. Patients were transferred to post anaesthesia care unit and were monitored. Post operatively sedation, nausea, retching, vomiting and complete response was assessed for 24hrs at the following intervals. 0-4hrs, 4-8hrs, 8-12hrs and 12-24hrs. The assessor was unaware of the study drug. Sedation was evaluated using Ramsay Sedation Score. Nausea was defined as unpleasant sensation associated with awareness of the urge to vomit. Retching was defined as the labored spastic, rhythmic contraction of the respiratory muscles without the expulsion of the gastric contents. An emetic episode was defined as one or more instances of forceful expulsion of gastric contents that occurred in rapid sequence of less than 1 minute between episodes. If there was two or more episodes of PONV in 24hrs, rescue antiemetic was given. Complete response (free from emesis) was defined as no PONV and no need for any rescue medication.

Results

In our study both the groups were comparable with respect to age, sex, body weight, duration of surgery and anaesthesia. The observations were statistically not significant with $p>0.05$ (Table 1).

Table 1: Comparison of demographic data between two groups.

Parameters	*Group A (Olanzapine) (N= 60)*	*Group B (Ondansetron) (N=60)*	*p value*
Age in years	42.95±14.374	45.05±13.684	0.416
Wt (kg)	58.22±10.2	60.36±13.3	0.42
ASA I: II	43:17	44:16	1
Duration of anaesthesia	132.8±52	130.2±54.4	0.78
Duration of surgery	99.3±24.2	100.2±34.2	0.45

Our study showed no statistical difference in the incidence of nausea during 0-4hrs and 4-8hrs. However there was a statistical difference between the groups in post op nausea at 8-12hrs and 12-24hrs (Table 2).

Table 2: Post op nausea comparison between two groups at different periods of follow-up.

Duration	*Postop nausea Group A(Olanzapine)*		*Postop nausea Group B (Ondansetron)*		*p value*
	Yes	*No*	*Yes*	*No*	
0-4hr	5 (8.3%)	55 (91.7%)	2 (3.3%)	58 (96.7%)	0.243
4-8hr	2 (3.3%)	(58 96.7%)	1 (1.7%)	59(98.3%)	0.559
8-12hr	2 (3.3%)	58 (96.7%)	8 (13.3%)	52 (86.7%)	0.048*
12-24hr	1 (1.7%)	59 (98.3%)	7 (11.7%)	53(88.3%)	0.028*

There was no statistical difference in the incidence of retching between the two groups at 0-4hrs and 4-8hrs. However the incidence of retching was significantly low in olanzapine group compared to ondansetron group at 8-12hrs and at 12 -24hrs (Table 3).

Table 3: Comparison of post op retching between two groups at different periods of follow-up.

Duration	*Postop retching*				*p value*
	Group A (Olanzapine)		*Group B (Ondansetron)*		
	Yes	*No*	*Yes*	*No*	
0-4hr	2 (3.3%)	58 (96.7%)	0	60(100.0%)	0.154
4-8hr	2 (3.3%)	58 (96.7%)	0	60(100.0%)	0.154
8-12hr	0	60(100.0%)	4 (6.7%)	56(93.3%)	0.042*
12-24hr	0	0.0%	12(20%)	48(80.0%)	<0.001*

The incidence of vomiting also showed no difference between groups at 0-4hrs and 4-8hrs, but we observed a significant less incidence of post op vomiting in olanzapine group compared to ondansetron group at 8-12hrs and 12-24hrs (Table 4).

Table 4: Post op vomiting comparison between two groups at different periods of follow-up.

Duration	*Post op vomiting*				*p value*
	Group A (Olanzapine)		*Group B (Ondansetron)*		
	Yes	*No*	*Yes*	*No*	
0-4hr	3 (5%)	57 (95.0%)	1 (1.7%)	59 (98.3%)	0.309
4 8 hr	2 (3.3%)	58 (96.7%)	0 (0%)	60(100.0%)	0.154
8 -12hr	0 (0%)	60 (100.0%)	4 (6.7%)	56 (93.3%)	0.042*
12 -24 hr	0 (0%)	60 (100.0%)	7 (11.7 %)	53 (88.3%)	0.006*

There was a significant difference in the use of rescue drug at 8 to 12 hrs. 6.7% of patients required rescue drug in ondansetron group whereas none of the patients received in the olanzapine group (Table 5).

Table 5: Rescue drug comparison between two groups at different periods of follow-up.

Duration	*Rescue drug given*				*p value*
	Group A (Olanzapine)		*Group B (Ondansetron)*		
	Yes	*No*	*Yes*	*No*	
0-4	2 (3.3%)	58 (96.7%)	0	60(100.0%)	0.154
4-8 hr	1(1.7%)	59(98.3%)	0	60(100.0%)	0.315
8-12hr	0	100.0%	4(6.7%)	56(93.3%)	0.042*
12-24hr	0	100.0%	1(1.7%)	59(98.3%)	0.315

Our study showed a significant increase in the incidence of drowsiness in the olanzapine group where dizziness and headache were comparable between the groups. (Table 6).

Table 6: Comparison of side effects between two groups.

	Side effects				*p value*
	Group A (Olanzapine)		*Group B (Ondansetron)*		
	Yes	*No*	*Yes*	*No*	
Drowsiness	10(16.7%)	50 (83.3%)	0	60(100.0%)	0.001*
Dizziness	1 (1.7%)	59(98.3%)	2 (3.3%)	58(96.7%)	0.559
Headache	1 (1.7%)	59 (98.3%)	2 (3.3%)	58 (96.7%)	0.559

Discussion

Postoperative nausea and vomiting (PONV) is a distressing side effect after anesthesia. Laparoscopic surgeries are associated with 40%-75% incidence of PONV [5]. Scinclair et al described female gender, previous history of PONV, motion sickness, nonsmoking, surgical procedure, type of anesthesia and surgery as the important risk factors for postoperative nausea and vomiting [6]. Nausea and vomiting is one of the important cause of patients discomfort in the postoperative period following laparoscopic surgeries [7]. As the number of laparoscopic surgeries are increasing, an effective prophylactic drug is highly desirable for patients satisfaction and early discharge.

5-HT3 receptors antagonists are routinely used to prevent postoperative nausea and vomiting in the surgical patients. Ondansetron, is a gold standard antiemetic among them. Olanzapine activity at multiple receptors suggests that it may have significant antiemetic properties. In this study we evaluated the antiemetic efficacy, safety and use of prophylactic olanzapine in preventing postoperative nausea and vomiting and compared it with ondansetron.

Tramer et al., assessed the efficacy, dose-response, and safety of ondansetron in prevention of postoperative nausea and vomiting and concluded that oral ondansetron 16 mg as the optimal fixed dose for preventing PONV [8]. Inter dose comparison of olanzapine for prevention of PONV by Ibrahim et al showed that 10mg was significantly better than 5mg for complete control of emesis [9]. In the present study we have selected olanzapine 5 mg and ondansetron 16 mg orally.

In our study the incidence of nausea was comparable between the olanzapine and ondansetron group in the 0-4hrs and 4-8hrs. However in the next 8-12hrs and 12-24hrs the patients who received olanzapine showed a significant decrease in the occurrence of nausea when compared to patients who received ondansetron. Similar results were seen in the incidence of retching and vomiting with no significance between the groups in the 0-4hrs and 4-8hrs and olanzapine group showing a significant decrease in retching and vomiting when compared to ondansetron during the 8-12hrs and 12-24hrs. Our results were similar to the study done by Ibrahim M et al who showed olanzapine to be better in controlling PONV in the late postoperative period. Many studies had showed the efficacy and safety of olanzapine in controlling nausea and vomiting in patients receiving high and moderate chemotherapy [10-12].

In our study, use of antiemetic was significant in the ondansetron group during the 8-12hrs when compared to olanzapine group.

A recent consensus from the Society of Ambulatory Anesthesia recommends prophylactic anti-emetic for patients undergoing abdominal surgeries with any

of the following risk factors-female gender, history of PONV, opioid use [13]. Therefore we have included female patients in our study.

In this study, olanzapine 5mg was associated with significant drowsiness. Patient who had drowsiness was monitored both preoperatively and postoperatively and oxygen 6lt/min was supplemented through face mask. However studies done by Ibrahim M et al., has showed no significant drowsiness among patients who received 5 mg or 10mg of olanzapine. Other side effects like dizziness and headache were not significant between groups [14, 15].

Limitations: Study had also some limitations including the duration of patient follow-up. If the duration of follow-up were longer, more accurate results would be obtained. And also present study was conducted on a limited number of cases and is inadequate to provide conclusive data.

Conclusion

The understanding of PONV mechanism and careful assessment of risk factors helps in PONV management. PONV prophylaxis should be considered for patient with moderate to high risk patients. In our study we concluded that Olanzapine 5 mg can be used safely and effectively for prophylaxis against PONV and we found it more effective in late post-operative period in preventing PONV compared to ondansetron.

Conflicts of interest

Authors declare no conflicts of interest.

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