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Prevention of Post-operative Nausea and Vomiting in Laparoscopic Cholecystectomy: A Comparison of Metoclopramide and Ondansetron

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Abstract

Background: Post-operative nausea and vomiting (PONV) is a frequent complication associated with laparoscopic cholecystectomy. In this randomized double-blind placebo controlled prospective study, we compared the efficacy of intravenous metoclopramide and ondansetron for prevention of PONV following laparoscopic cholecystectomy in patients. *Materials and Methods:* A total of 75 patients (*20–60 years of age*) undergoing elective laparascopic cholecysetectomy were randomly allocated to one of the three groups of 25 patients each. Group A received metoclopramide *10 mg,* Group B received ondansetron and group C received normal saline *10 ml* after induction. All episodes of PONV within 24 hrs. after induction of anesthesia were recorded. *Results:* The overall incidence of post-operative emesis was 44% in control group, 16% in Metoclopramide group and 12% in Ondansetron group.The decrease in incidence of emesis in Metoclopramide and Ondansetron group was significant as compared to control group whereas there was no statistical difference between Metoclopramide and Ondansetron groups. *Conclusion:* For prevention of PONV after laparoscopic cholecystectomy, both metoclopramide and ondansetron are equally effective in comparison to placebo group.

Keywords: Laparoscopic cholecystectomy; Ondansetron; Metoclopramide; Post-operative nausea and vomiting.

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Introduction

Post-operative nausea and vomiting (PONV) has been one of the most distressing accompaniments of surgery and anesthesia, with an incidence of approximately 30%.[1] However, a higher incidence rate of 46% to 75% has been reported in patients after laparoscopic cholecystectomy.[2–4] This has been attributed tomechanical factors like pressure on the stomach and gut due to pneumoperitoneum as well as chemical factors like influence of carbon dioxide. Although nausea and vomiting can result in dehydration, electrolyte imbalances and delay in discharge from hospital but for the anesthesiologists, the most dreaded complication is the pulmonary aspiration of vomitus especially when airway reflexes are depressed due to the residual effects of anesthetic drugs.

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Various drugs and techniques have been employed in the past for the prevention of PONV but the search for better anti-emetics is still going on.[5,6] Metoclopramide is the routine drug being used for prevention of PONV for the last *30 years* due to its various favorable properties.[7] The anti-emetic action of metoclopramide is due to the antagonism of D_2 receptors centrally and peripherally. The inhibition of chemoreceptor trigger zone (CTZ) in the central nervous system prevents nausea and vomiting triggered by many stimuli. It also exhibits a gastrokinetic effect by increasing selective cholinergic response of gastrointestinal tract by inhibiting gastric smooth muscle relaxation. The tone of lower oesophageal sphincter is also increased thus decreasing the risk of aspiration. However, higher doses can lead to extrapyramidal side effects. In the recent years, interest has been focused on a new $5HT^3$ receptor specific antagonist, Ondansetron which does not act on other receptors like dopaminergic, histaminic, cholinergic etc. and so has few side effects.[8]

Therefore, this study was planned to evaluate the effectiveness of ondansetron and metoclopramide in preventing PONV in patients undergoing laproscopic cholecystectomy.

Materials and Methods

This study was carried at Government Medical College in Punjab after obtaining approval from ethical committee. The study was conducted on 75 adult patients of both sexes in age group of *20–60 years* of ASA grade I and II undergoing elective laparoscopic cholecystectomy. Before enrolment to the study, awritten informed consent was obtained from patients. Criteria for exclusion were obese patients (> 20% expected body weight for their age), patients with history of motion sickness, chronic steroid therapy or having had anti-emetics within last *24 hours* before surgery. Patients with chronic exposure to nicotine and having any disease that could prolong gastric emptying or make them prone to vomiting *e.g.*, diabetes, hiatus hernia were not included in the study.

Random allocation was decided on the basis of computer generated random number table. The coded slips were prepared and put in envelop and according to the slip, solution was prepared by independent observer not taking part in study.

Group A (n = 25) received injection metoclopramide *10 mg* I.V. diluted to make volume of *4 ml*.

Group B (n = 25) received injection ondansetron *4 mg* I.V. diluted upto *4 ml*. Group C (n = 25) received *4 ml* normal saline.

All the patients were subjected to a thorough pre-anesthetic checkup a day prior to surgery and relevant investigations were done. The patients were given tablet Diazepam *10 mg* on the night before surgery. After bringing patient to the O.T, I.V. cannula was placed and monitors were attached. Inj. Butorphanol *1 mg* and inj. Atropine *0.6 mg* were used for intravenous (I.V.) pre-medicantion. All patients were induced with inj. Thiopentone *5 mg/kg* and suxamethnoium *2 mg/kg* I.V. The study drug was given soon after intubation. During IPPV using bag and mask ventilation, low airway pressures were maintained.

Anesthesia technique employed was same in all patients using halothane, nitrous oxide, oxygen and vecuronium. Before extubation, patients received Inj. Diclofenac *75 mg* intra-muscularly.

Intra-operatively, continuous monitoring of patient's heart rate and blood pressure were done. Post-operatively, patients were monitored every hour for the first *4 hours* and then at *24 hours*. All episodes of nausea and vomiting were recorded during first *24 hours* after general anesthesia. 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.

Nausea was measured by 11 points numerical visual analog scale with 0 = no nausea and 10 = nausea as bad can be. A score of more than 5 was considered severe, 5 = moderate and 4 or less was considered minimal. Moderate or severe nausea was considered as major nausea. The numbers of vomiting episodes were counted and more than 2 episodes were counted severe, 2 episodes as moderate and less than 2 considered mild vomiting. Patients who had more than 2 episodes of vomiting were given inj. Metoclopramide *10 mg* I.V. as a rescue anti-emetic.

Results

All the 75 patients, 25 in each group were included in the study. There were no significant differences between the three groups with regard to age, weight and duration of surgery as shown in (**Table 1**). Intra-operative vital score was 1.88 ± 0.33, 1.92 ± 0.28 and 1.84 ± 0.37 in group A, B and C respectively. This was statistically in-significant. The post-operative

vital scores were almost similar in all groups. At no time, difference in the post-operative vital score was significant between the groups as shown in (**Table 2**). Nausea was experienced by 17 patients of control group (68%) while it was reported in 8 patients of Metoclopramide group (32%) and 9 patients of Ondansetron group (36%) respectively displays (**Fig. 1**). The mean maximum nausea severity score was 1.68 ± 2.97 in the metoclopramide group, 1.68 ± 2.98 in the ondansetron group and 4.28 ± 3.92 in the control group shows (**Table 3**). This difference was statistically significant between control versus (*v/s*) metoclopramide group ($p < 0.05$) and control *v/s* ondansetron group ($p < 0.05$) but statistically in-significant on comparison of metoclopramide *v/s* ondansetron groups ($p > 0.05$). In our study, metoclopramide was found to be more effective in decreasing severity of early nausea (0–2 hours) while ondansetron proved better as far as control of late nausea (2–24 hours) was concerned as shown in (**Tables 4 & 5**).

Table 1: Patient characteristics

Variables Mean ± SD	Group A (n = 25)	Group B (n = 25)	Group C (n = 25)
Age (y) ± SD	39.96 ± 10.69	40.36 ± 7.78	39.08 ± 9.42
Weight (kg) ± SD	63.16 ± 9.47	64.26 ± 11.20	63.48 ± 10.61
Duration of surgery (min)	56.00 ± 13.69	57.40 ± 14.44	53.60 ± 12.71

Table 2: Mean vital scores

	Group A	Group B	Group C
IVS	1.88 ± 0.33	1.92 ± 0.28	1.84 ± 0.37
PVS-0HR	1.84 ± 0.37	1.92 ± 0.28	1.92 ± 0.28
PVS-1HR	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00
PVS-2HR	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00
PVS-3HR	2.00 ± 0.00	1.96 ± 0.20	2.00 ± 0.00
PVS-4HR	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00
PVS-4-24HR	2.00 ± 0.00	2.00 ± 0.00	2.00 ± 0.00

IVS-Intra-operative vital score; PVS-Post-opeartive vital score; HR-Hour.

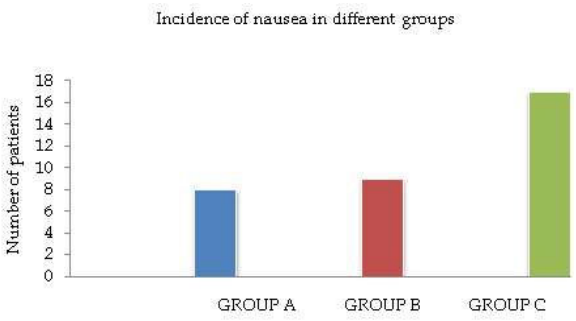

Fig. 1: Incidence of nausea in different groups

Table 3: Post-operative nausea score at different time intervals

Time (Hours)	Group		
	Metoclopramide	Ondansetron	Control
0	0.12 ± 0.44	0.08 ± 0.28	0.24 ± 0.52
1	0.56 ± 1.19	0.72 ± 1.24	1.04 ± 1.21
2	1.32 ± 2.46	1.04 ± 2.17	2.68 ± 2.69
3	1.48 ± 2.90	1.08 ± 2.63	2.96 ± 3.35
4	0.44 ± 0.92	0.72 ± 2.21	1.76 ± 3.28
4–24	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Max. Mean Severity Score	1.68 ± 2.97	1.68 ± 2.98	4.28 ± 3.92

The overall incidence of post-operative emesis was 44% in control group (11/25), 20% in Metoclopramide group (5/25) and 12% in Ondansetron group (3/25) (**Fig. 2**). The decrease in incidence of emesis in Metoclopramide and Ondansetron group was significant as compared to control group whereas there was no statistical difference between Metoclopramide and Ondansetron groups. However, during early period (0–2 hours) the incidence of vomiting was 4% in metoclopramide group as compared to 12% in both ondansetron and control group while it increased to 20% in metoclopramide and 40% in control group as compared to 8% in ondansetron group during late period (2–24 hours). No significant untoward side effects were seen in any of the three groups as

Table 4: Post-operative emesis at different time intervals

Time (Hours)	Group								
	Metoclopramide			Ondansetron			Control		
	No.	%	Mean	No.	%	Mean	No.	%	Mean
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	1	4	0.04 ± 0.20	3	12	0.12 ± 0.33	3	12	0.12 ± 0.33
3	4	16	0.16 ± 0.47	2	8	0.08 ± 0.28	8	32	0.32 ± 0.48
4	4	16	0.16 ± 0.37	2	8	0.08 ± 0.28	10	40	0.40 ± 0.71
4–24	1	4	0.04 ± 0.20	1	4	0.04 ± 0.20	5	20	0.20 ± 0.50

Metoclopramide *v/s* ondansetron - not significant;

Control *v/s* metoclopramide - not significant;

Control *v/s* ondansetron - highly significant at *3 hours and 4 hours.*

shown in (**Table 6**).Use of rescue treatment shown in (**Fig. 3**) was similar in metoclopramide and ondansetron group (8%) while it was was higher in control group (24%).

Table 6: Incidence of side effects

	Headache	Dryness of mouth	Sedation	Any other
Group A	1	1	1	1
Group B	2	2	0	1
Group C	1	2	0	1

Discussion

Despite scientific advances in anesthesia and surgery, nausea and vomiting are among the most common distressing post-operative complications. The etiology of PONV after laparoscopic cholecystectomy is multifactorial. Anesthetic factors like the type of pre-medication, amount of gastric distension, suctioning, anesthetic drugs, anesthetic technique and post-operative pain increase the incidence of PONV. Various non-anesthestic factors like age, gender, weight, history of motion sickness, anxiety, gastroparesis etc. also pre-dispose patients to PONV.[9] In our study, patients were similar in terms of demographic variables, duration of surgery and basic vital signs. Patients with low threshold for vomiting like gastroparesis, motion sickness etc. were excluded from our study. Anesthetic drugs and the technique used were kept similar in all groups.

In the present study, the overall incidence of nausea was 68% in control group while it was 32% in metoclopramide group and 36% in ondansetron group which was statistically in-significant

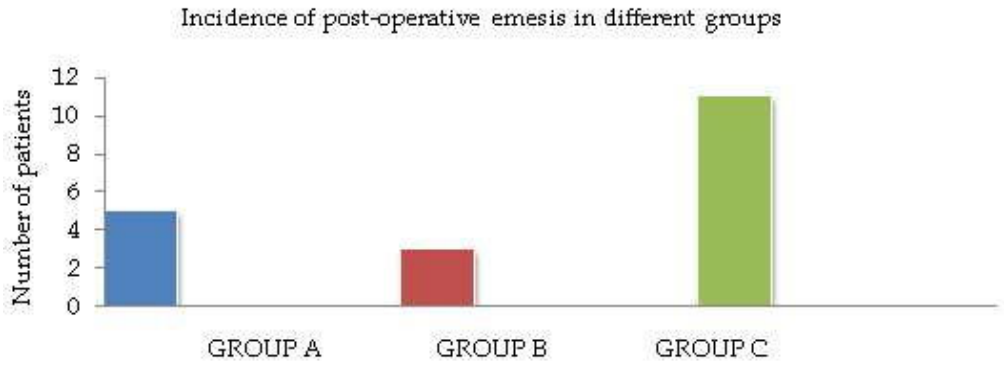

Fig. 2: Incidence of post-operative emesis in different groups

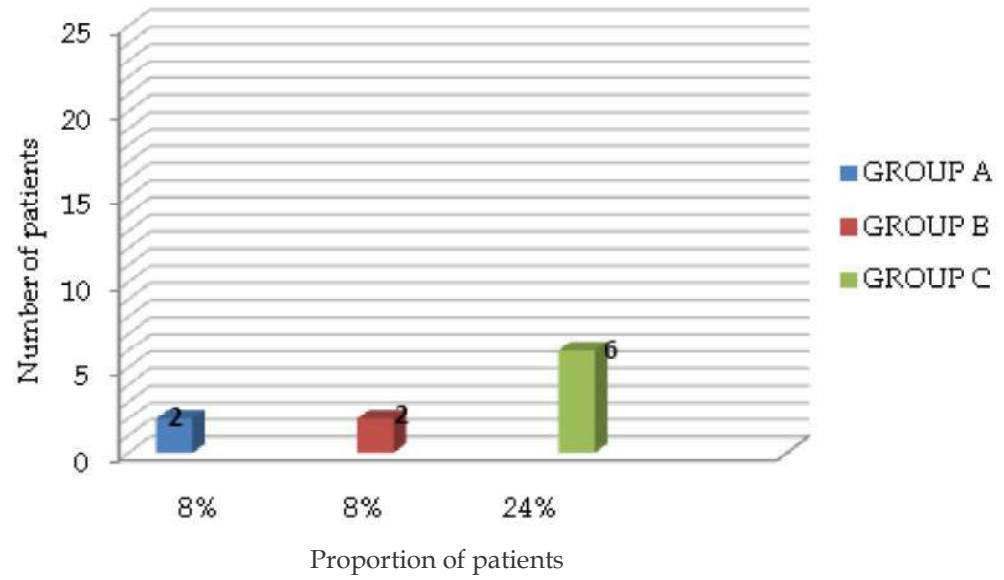

Fig. 3: Incidence of use of rescue treatment in different groups

amongst metoclopramide and ondansetron group but signifant for both groups in comparison with control group. Incidence of post-operative emesis was 44% in control group (11/25) which was significant ($p < 0.001$) when compared to 20% in Metoclopramide group (5/25) and 12% in Ondansetron group (3/25) thus showing that the incidence of post operative vomiting was maximum in control group. As per our results, the frequency of emesis was less in the ondansetron group but it was not statistically significant when compared to the metoclopramide group. These results are in concordance with the studies by Wilson *et al.* and Bilgin TE *et al.* who proved a significant decrease in the incidence of vomiting in the ondansetron and metoclopramide groups as compared to the control group without any statistical difference amongst themselves.[10,11] K Isazadehfar[12] concluded that both metoclopramide and ondansetron are equally effective for prevention of vomiting butfor prevention of nausea, ondansetron is more effective than metoclopramide.

In a similar research, Quanyor and Raedar showed the overall incidence of post-operative nausea and vomiting to be almost similar in metoclopramide and ondansetron groups. Incidentally, they also observed a greater incidence of moderate to strong pain during the post-operative period in the ondansetron group as compared to the metoclopramide group.[13]

Farhat K *et al.* on the other hand, stated that the frequency of nausea and vomiting was clinically and statistically lower in ondansetron group as compared to the metoclopramide group ($p = 0.035$) while the use of rescue anti-emetic was significantly higher in the latter ($p = 0.022$).[14] These findings were also reinforced in a meta analysis by Wu SJ *et al.*, where the total incidence of post-operative nausea and vomiting within 24 hours after laparoscopic cholecystectomy was 31% in the ondansetron group and 56% in the metoclopramide group thus indicating ondansetron to be a better anti-emetic.[15]

In the present study, we found the incidence of 'early nausea' to be 28% and 36% in metoclopramide and ondansetron group respectively as compared to 64% in control group. The incidence of 'late nausea' was 32% for metoclopramide group, 24% for ondansetron group and 60% for control group. Thus it shows that ondansetron is more effective for 'late nausea' than metoclopramide. It also decreases severity of 'late nausea' as compared to Metoclopramide. The decreased effect of metoclopramide on 'late nausea' may be due to its shorter duration of action. Masoomeh Tabari *et al.*[16] in their study concluded that Ondansetron was more effective than dexamethasone and metoclopramide in preventing vomiting after laparoscopic cholecystectomy at intervals of *0–1* and *1–6 hours* and also delayed the onset of nausea and vomiting.

Many studies reported that ondansetron is statistically superior to metoclopramide for prevention of PONV.[17–19] In our study too, ondansetron group has low frequency of emesis although it was statistically insignificant. Other published studies that evaluated the efficacy of ondansetron and metoclopramide administered intravenously have shown similar reductions in the incidence of PONV during the *24 hrs.* post recovery period.[20,21] Though we encountered very few and mild side effects with regard to all groups, Daria and Kumar stated that metoclopramide not only has a low (36.7%) success rate in the prevention of PONV, but also a higher incidence of side effects. However, they also discredited the efficacy of ondansetron for the prevention of PONV.[22]

Conclusion

Ondansetron *4 mg* and metoclopramide *10 mg* are both almost equally effective as prophylactic anti-emetics for the prevention of post-operative nausea and vomiting in laparoscopic cholecystectomy procedures under general anesthesia as compared to placebo with minimal side effects.

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