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Original Research Article

Study of the effect of timing of pre-operative administration of dexamethasone and ondansetron on post-operative nausea and vomiting follow laparoscopic cholecystectomy: A prospective randomized control trial

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ABSTRACT

Background: Post-operative nausea and vomiting (PONV) is potential complication in patients after laparoscopic cholecystectomy. The incidence rate of PONV after laparoscopic cholecystectomy (LC) is 46-75% which is higher than that after other types of surgery. The present study was aimed to compare the effect of timing of dexamethasone and ondansetron alone when given 45 minutes before induction or given just before induction of anaesthesia for control of PONV in laparoscopic cholecystectomy.
Aim: Tocompare the effect of timing of dexamethasone and ondansetron each when given 45 minutes before induction or given just before induction for control of PONV in laparoscopic cholecystectomy.
Materials and Methods: After approval by the institutional ethics committee, this study was carried out on 200 patients of both sexes in the age group of 20-60 years. It was a randomized controlled trial. And after obtaining the consent, the patients were allocated in four groups randomly. Group A: 8 mg dexamethasone 45 minutes before induction, Group B: 4 mg ondansetron 45 minutes before induction, Group C: 8 mg dexamethasone just before induction and Group D:4 mg ondansetron just before induction. Patients were observed for 24 hours after surgery for any episode of nausea and vomiting for 24 hours. Patient satisfaction with the management of PONV symptoms using 10 points verbal rating scale was accessed (VRS, 0=not satisfied, 10 = fully satisfied).
Results: Incidence of nausea and vomiting was significantly higher in group B was 68% and D 50% in comparison to group A 28%and C 36% (P=0.003). PONV score was highly significant when ondansetron was administered 45 minutes before induction as compare to dexamethasone when administered 45minutes before induction. The effect of ondansetron was also significant in PONV score of 24 hrs in comparison to dexamethasone.
Conclusion: The ondansetron appears to have a shorter duration of action in comparison to dexamethasone. Timing of administration of ondansetron is important in laparoscopic cholecystectomy before surgery as it has bearing on the incidence of vomiting and rescue antiemetic required. It was found that administration of ondansetron just before induction still delays the onset of PONV in comparison to when given 45 minutes before induction.

1. Introduction

Post-operative nausea and vomiting (PONV) are potential complications in patients after laparoscopic cholecystectomy.[1,2] An incidence of 46-75% has

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been reported in patients undergoing laparoscopic cholecystectomy who did not receive any antiemetic medication.[1–3] The factors which result in the increased incidence of PONV are patient characteristics, surgical procedure, anaesthesia technique, and postoperative care.[4,5] Surgical factors particularly in LC have intraperitoneal insufflation of CO2, leading to stretching of peritoneum and subsequent nausea and vomiting.[6] The factors which increase PONV after LC includes pain, dizziness, ambulation, oral intake, and opioids. Dexamethasone is an inexpensive and effective antiemetic drug with minimal adverse effects after a single-dose administration.[6]

Recent interest has been focused on the use of various antiemetics, acting at different receptors at a specific time during surgery. It has been seen that ondansetron is more effective in the initial hours of the postoperative period and dexamethasone is found to be more effective in the late postoperative period after surgery.[7] The present study was aimed to compare the effect of timing of dexamethasone and ondansetron alone when given 45 minutes before induction or given just before induction of anaesthesia for control of PONV in laparoscopic cholecystectomy.

2. Materials and Methods

The randomized controlled trial study was carried out in tertiary care centre after approval by the institutional ethics committee. This randomization and group allocation were computer generated by non study related anaesthetic. The anaesthesia provider gave drug to patient according to the group of patients. The observer was blinded to the drugs infused. However, in case of any untoward reaction or complication in postoperative period the code of the drug was opened and the patient /subject was excluded from the study. It was documented in the patients file and study proforma. After literary review the study was carried out on 200 patients of ASA I –II scheduled for elective laparoscopic cholecystectomy of both sexes in the age group of 20-60 years with 95% confidence level and power of study as 80%. The patients with previous history of PONV and motion sickness were excluded. The following patients who were on anti-emetic treatment, or are active smoker or with history of gastro oesophageal reflux disease were also excluded. After obtaining the consent, the patients were allocated in four groups randomly:Group A**:** 8 mg dexamethasone 45 minutes before induction, Group B**:** 4 Mg ondansetron 45 minutes before induction, Group C: 8 mg dexamethasone just before induction, Group D: 4 mg ondansetron just before induction.

This randomization and group allocation were computer generated and the anaesthesia provider gave drug to patient according to the group of patients. The observer was blinded to the drugs infused. However, in case of any untoward reaction or complication in postoperative period the code of the drug was opened and the patient /subject was excluded from the study. Informed consent was taken from the patients after a detailed explanation of the study. The patients were explained on the use of verbal rating scale (VRS, 0= not satisfied, 10=fully satisfied) and were instructed for overnight fasting. After routine premedication 18G i.v. cannula was secured in preoperative room in all the patients and normal saline was started as intravenous fluid and patients were given drugs according to the group allocated by anaesthesia provider. All patients were subjected to routine monitoring and routine general anaesthesia with injection bupivacaine(1.25%) was given locally for post-operative analgesia before the closure as per dose of 2mg/kg After reversal, the patient was shifted to postoperative recovery room. All patients were administered inj. diclofenac 75 mg, 8 hourly as post-operative analgesic along with proper documentation. Patients were observed for 24 hours after surgery for any episode of nausea and vomiting every one hourly for two hours and six hourly for 24 hours. The severity of postoperative nausea and vomiting was assessed on a Numerical rating scale. (NRS 0-3) with score 0 of no nausea and no retching, and score 3 of vomiting >2 times in 30 minutes. Rescue antiemetic inj metoclopramide 10 mg iv was given to the patients with a PONV score of ≥2 or on the demand of the patient. Patient satisfaction with the management of PONV symptoms using 10 points verbal rating scale was accessed (VRS, 0=not satisfied, 10=fully satisfied. The data were recorded into an excel sheet and exported to SPSS software (v21.0; IBM, USA). Categorical variables were presented as frequency and percentages and compared using Chi-Square test. Quantitative variables were expressed as mean and SD, and compared using one-way ANOVA followed by Bonferroni's post-hoc correction. P-value <0.05 was considered significant.

3. Results

Demographic and baseline vitals were comparable in all the four groups (Figure 1). There was no significant difference in age between different groups of the patients (P=0.551).

Patients were observed for 24 hours after surgery for any episode of nausea and vomiting every one hourly for two hours and six hourly for 24 hours. The severity of postoperative nausea and vomiting was assessed on a Numerical rating scale. (NRS 0-3) with score 0 of no nausea and no retching, and score 3 of vomiting >2 times in 30 minutes.

The incidence of PONV over period of 24hrs in group A (dexamethasone 8 mg 45 minutes before induction) was 28%, in group B (ondansetron 4 mg 45 minutes before induction) was 68%, in group C (dexamethasone 8 mg just before induction) was 36%, and in group D (ondansetron 4 mg just before induction) was 50% patients. Incidence of nausea and vomiting was significantly higher in group B and D in comparison to group A and group C (P=0.003).

Table 1: Comparison of PONV score at baseline between groups

	Group A (n=50)	Group B (n=50)	Group C (n=50)	Group D (n=50)
No nausea and vomiting	50	45	50	46
Complaining of sickness and retching	0	3	0	2
Vomiting once or twice in 30 minutes	0	1	0	1
Vomiting >2 times in 30 minutes	0	1	0	1
P value		0.364#		

Data presented as numbers

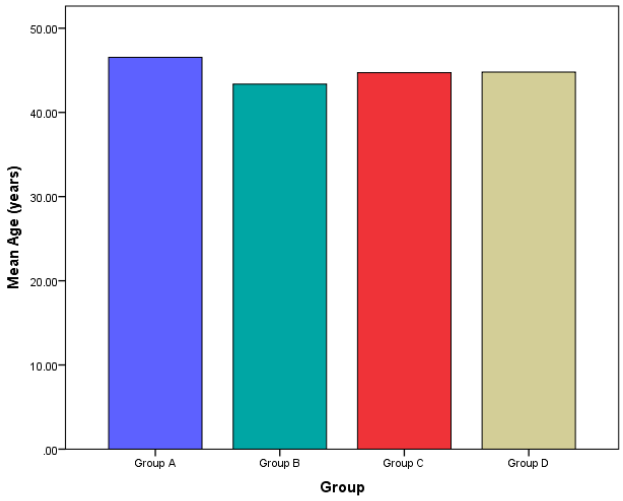

Fig. 1: Comparison of age between groups

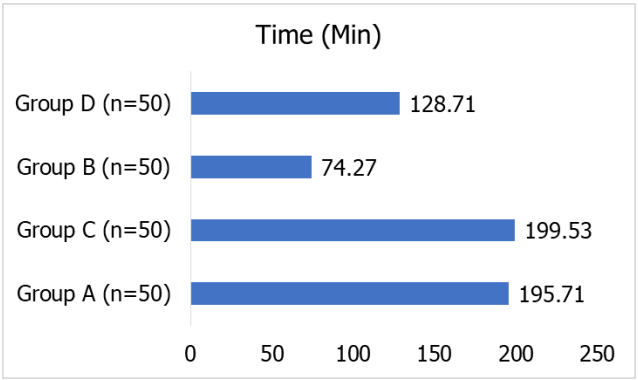

Fig. 2: Time to first rescue antiemetic

PONV score at 24 hours between all four groups was highly significant.

It was observed that time to first rescue antiemetic from the start of surgery was significantly lower in group B and D in comparison to group A and C(P<0.0001). The result of the comparison of time to first rescue antiemetic among all four groups was very highly significant. The total number rescue antiemetics given to patients in group A, B, C and D was 16, 45, 18, and 32 respectively. The results of the comparison of the total number of doses of rescue antiemetic among all four groups were significant.

4. Discussion

Post-operative nausea and vomiting (PONV) are potential complications in patients after laparoscopic cholecystectomy. The incidence rate of PONV after laparoscopic cholecystectomy (LC) is higher than that after other types of surgery.[8] PONV is the second most common complaint after pain being the most common.[9] PONV remains an important problem in modern anaesthesia because of the multitude of consequences such as delayed recovery, unplanned hospital admission, pulmonary aspiration, dehydration, wound dehiscence and prolonged hospital stay. The present study was aimed to compare the effect of timing of dexamethasone and ondansetron alone when given 45 min before induction or given just before induction for control of PONV in laparoscopic cholecystectomy.

The dexamethasone proved to be far more efficacious in preventing PONV compared to ondansetron when given pre-emptively. Dexamethasone when given 45 minutes before induction the incidence of PONV was twenty-eight percent whereas when ondansetron was given 45 minutes before the incidence of PONV was sixty-eight percent. The study by Gupta et al also concluded that role of pre-operative dexamethasone given 90 minutes before surgery as prophylaxis for PONV in laparoscopic surgery was also more effective in comparison to ondansetron.[10]

The incidence of PONV was 36% in dexamethasone group as compare to ondansetron group which was 50% when given at the time of induction along with other induction agents. D'Souza et al[11] conducted study with different doses of dexamethasone that is 4 and 8mg and also compared it with 4mg of ondansetron, and he observed that 4mg of dexamethasone was most efficacious as compared to other groups. Also, the incidence of PONV was highest with ondansetron especially in first 3 hours of post-operatively. The incidence of request for rescue antiemetic was significantly lower in dexamethasone 4mg group as compared to other groups i.e., 0% as compared to the 6.7%

Table 2: Comparison of overall PONV score at 24 hours between groups

	Group A (n=50)	Group B (n=50)	Group C (n=50)	Group D (n=50)
No nausea and vomiting	36	16	42	25
Complaining of sickness and retching	9	22	13	16
Vomiting once or twice in 30 minutes	3	9	5	6
Vomiting >2 times in 30 minutes	2	3	0	3
P value		0.003**		

Data presented as numbers

Table 3: Rescue antiemetics (total number of doses)

	Group A (n=50)	Group B (n=50)	Group C (n=50)	Group D (n=50)
Baseline	0	5	0	5
2-hour	6	6	7	5
4-hou	3	13	4	6
6-hour	6	7	5	2
12-hour	1	9	2	9
18-hour	0	5	0	5
24-hour	0	0	0	0
Total	16	45	18	32
P value		0.026*		

and 16.1% in the dexamethasone 8 mg and ondansetron 4 mg group respectively.

The incidence of PONV was significantly less when given 45 minutes before induction as compare to when given just before induction when given along with other induction agents. Wang et al. also concluded that requirement of rescue antiemetic is much less when dexamethasone is given before induction than as compare to when dexamethasone is given at the end of surgery.[12,13]

In contrast, to dexamethasone group, the requirement of rescue antiemetic is less when ondansetron is given just before induction agent as compare to when it is given 45 minutes before the induction. So, it was concluded that ondansetron is short acting drug which was also approved by the study conducted by Cruz et al. who, concluded that the best time to administer injection ondansetron is 30 minutes before the completion of surgery than to administer it at the time of induction.[14] Sun et al, also concluded that the administration of ondansetron at the end of surgery is most effective as compare to when it is administered at the time if induction.[15]

The prophylactic use of single dose of dexamethasone has been found to be in reducing the incidence of PONV during 24 hours after laparoscopic cholecystectomy. In contrast, ondansetron is found to be effective in reducing the incidence of PONV after laparoscopic cholecystectomy up to maximum duration of 4 to 6 hours. With better understanding the pathophysiology of PONV and the pharmacology of drugs, the timing of these drugs seems important and logical in the management of PONV.

The limitations were that we included only ASA I and II patients with fixed intraoperative anaesthetic techniques in our study. ASA III and IV patients could not be included in view of ethical issues. For patients with certain diseases like diabetes and hypertension preoperative medication could not be stopped which also interfered with the incidence of postoperative nausea and vomiting.

5. Conclusion

Dexamethasone has a longer duration of action and better efficacy as antiemetic in comparison with ondansetron in the prevention of postoperative nausea and vomiting. The timing of administration of dexamethasone with reference to induction of anesthesia has no bearing on the incidence of vomiting and rescue antiemetic requirements. The ondansetron appears to have a shorter duration of action and is associated with a higher incidence of PONV in the first six hours in comparison to dexamethasone. Timing of administration of ondansetron is important in laparoscopic cholecystectomy before surgery as it has bearing on the incidence of vomiting and rescue antiemetic required.

6. Source of Funding

Nil.

7. Conflicts of Interest

There are no conflicts of interest.

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