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Research Article

Comparative Study on Ondansetron with Granisetron in the Prevention of Postoperative Nausea and Vomiting in Subjects Undergoing Laparoscopic Cholecystectomy Under General Anesthesia

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Abstract

Laparoscopic cholecystectomy leads to post-operative nausea and vomiting. This is cured by using antagonist of 5 HT-3 receptors present on enterochromaffin cells or vagus nerves terminals. It is of interest to compare the efficacy of ondansetron and granisetron in patients undergoing laparoscopic cholecystectomy. 40 patients of age between 18-58 years were selected, and divided into two groups where group A (n = 20) includes the patients administered with ondansetron (4mg) and group B (n = 20) includes the patients administered with granisetron (3mg). Patients were observed at a time interval of 0h, 1h, 2h, 6h, 12h and 24h postoperatively and the incidence of nausea, retching or vomiting and post operative nausea and vomiting (PONV) was measured using the visual analogue score (VAS). 10-30% (P = 0.05) of total post-operative patients were found with PONV in an initial 2h. As per VAS, 20-30% (P = 0.05) and 10-15% (P = 0.05) of post-operative patients in group A and B has an incidence of nausea, vomiting and PONV in initial 2h. respectively. After 24 hours, 60% (P = 0.05) of patients in group A and 70% (P = 0.05) in group B were free from emesis. Thus, the incidence of vomiting (20%) as compared to nausea (15%) and PONV (20%) are less in subjects who have received granisetron. Data showed that granisetron is a better antinausea drug.

Keywords: Ondansetron; Granisetron; Laparoscopic Cholecystectomy; PONV

Background

Distressing symptoms like postoperative nausea and vomiting (PONV) commonly occur after laparoscopic surgeries under general anesthesia [1]. PONV is said to have a multifactorial etiology [2] and researchers observed that reduced morbidity is associated with cholecystectomy by laparoscopic surgery [2] (an accepted procedure for symptomatic cholelithiasis), but this procedure has increased the incidence of PONV (53-72%) [3,4]. Carbon dioxide insufflation led to the dilatation of intentional loops and observed as a risk factor for nausea and vomiting after laparoscopic surgery. After the stimulation of gut wall-associated mechanoreceptors, serotonin is synthesized, which triggers the medulla's chemoreceptors, and finally, vagus nerve terminals are activated and evoke an emetic response [5,6].

Granisetron is first-generation, non-competitive, 5 HT-3 antagonists [7,8]. It is used as an anti-emetic drug [9]. It acts directly on enterochromaffin cells and acts solely through 5 HT-3 receptors on vagal afferents [9]. It crosses the placental membrane in a dose-dependent manner [10]. It is administered with various routes. It has similar efficacy compared to other first-generation 5HT-3 antagonists (tropisetron, ondansetron, and dolasetron) [11].

Ondansetron is also a first selective 5 HT antagonist and safest effective anti-emetic agents. It has a similar mechanism of action with granisetron [12,13]. It affects the vagus nerve terminals where 5-HT-3 are present. It is well known that the vagus nerve is responsible for the triggering of nausea and vomiting, and this drug is metabolised with the help of cytochrome P_{450} present in the liver [14,15].

It is suggested that the selection of both drugs over the other be based on comparison bases for the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anesthesia.

Therefore, we conducted a study to compare the efficacy of the 5 HT-3 antagonists i.e., granisetron against ondansetron, that has proven to be an effective and safest drug in preventing nausea and vomiting after laparoscopic cholecystectomy. This study aims to compare ondansetron with granisetron in preventing postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anesthesia.

Material and Methods

This randomised, cross sectional study was conducted at Pandit Jawaharlal Nehru Govt Medical College and Hospital Chamba HP, India. The said work was approved from the ethical committee of the same medical college. Each subject has given written consent and informed as per regulation of randomized, double-blind study. This study was conducted in a prospective, cross sectional and randomized fashion from July 2018 to Oct. 2018. Preoperative baseline values of heart rate and blood pressure and mandatory biochemical tests were recorded.

Forty subjects between 18-58 years were selected with ASA grade I-II (American society of Anesthesiologists) undergoing elective laparoscopic cholecystectomy under general anaesthesia [14]. We excluded subjects with any of the following symptoms like allergy to any drug, vomiting/retching/nausea/anti-emetic in 24h preceding administration of anesthesia. Subjects on chronic steroids, prokinetics, anti-emetic/ antacids, menstruating/ lactating or pregnant females, history of alcohol or substance abuse, subjects with chronic diseases, QT prolongation on preoperative electrocardiography.

As per the regulations of the computer based randomization technique, these subjects were equally divided into group A (n = 20) with ondansetron 4.0 mg (fixed-dose), group B (n = 20) with granisetron 0.75 mg (fixed dose). Care was taken on the preparation of study drugs with the use of identical syringes [16]. All practitioners who are working for this research work were blinded to the allocation of groups.

For randomized control study 40 patients of age between 18-58 years were selected and divided into two groups where group A (n = 20) includes the patients administered with ondansetron (4mg) and group B (n = 20) includes the patients administered with granisetron (0.75mg). Patients were observed at a time interval of 0h, 1h, 2h, 6h, 12h and 24h postoperatively and the incidence of nausea, retching or vomiting and PONV was measured using visual analogue score (VAS).

Anesthetics procedure

The patients were kept fasting after 10 PM a day before the surgery, and the baseline parameters were taken and recorded. Patients were anesthetised as per regulations under randomised control study. On arrival in operation theater, routine monitoring ECG, pCO_2 and baseline BP were recorded with the pulse oximeter.

The selected drugs were diluted with 10 ml of saline. The drug was given in period of 10 min as per the randomised schedule. The patient was induced after preoxygenation for 3 min with inj. Propofol with 10mg per Kg body weight and intubation with an appropriate size tube with injection Vecuronium bromide 0.1 mg per Kg body weight and anaesthesia were maintained with O_2:N_2O(50%:50%), Isoflurane (0.8-1.0%).

Muscle relaxation was maintained with boluses of injection Vecuronium bromide, and intermittent positive pressure with end-tidal CO_2 between 30-35mm Hg was maintained. A ryles tube was placed for emptying airs and secretions from the stomach. An IV line was maintained with ringer lactate solution 2.0 ml per Kg body weight. During the surgery, a strict watch was maintained in monitoring the intra-abdominal pressure (IAP) between 10-12 mm of Hg. At the end of the surgery, Ryle's tube was removed after doing suction. Injection glycopyrrolate and neostigmine were given as reversal to remove the residual neuromuscular block, and extubation was done after adequate neuromuscular reversal. Injection diclofenac sodium 1mg/kg body weight was administered IV half an hour before the end of the surgery.

An IV line was maintained, and intravenous crystalloids were given 2ml/kg body after the surgery, and the patient was kept post-anaesthesia care unit, and monitoring was continuously done.

Measurements [17]

Visual Analogue Score (VAS) was used to measure the pain intensity among the group[17]. Scale was divided into four points i.e. (0, none; 1, nausea; 2, retching; 3, vomiting). If VAS score will come greater than four after that rescue analgesia was provided with injection paracetamol (1gm/kg of body weight) intravenously. Importantly, headache, diarrhea, and dizziness was recorded to confirm the adverse effect of selected drugs.

Statistical analysis

Collected data were assessed using statistical package for the social sciences ver. 23.0® software where $p < 0.05$ was considered statistically significant. Results were expressed in mean ± standard deviation of the values, and chi-square test was performed among the groups to find out the efficacies between selected drugs.

Results

10-30% (P = 0.05) of total post-operative patients were found with PONV in an initial 2h. As per VAS, 20-30% (P = 0.05) and 10-15% (P = 0.05) of post-operative patients in group A and B has an incidence of nausea, vomiting and PONV in initial 2h. respectively. After 24 hours, 60% (P = 0.05) of patients in group A and 70%(P = 0.05) in group B were free from emesis.

The present study has been planned and performed to compare two drugs (ondansetron and granisetron) in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia. In the present study, 4.0 mg and 0.75mg of body weight of ondansetron and granisetron were used, respectively.

Table 1 presents the characterization of the study population by age, sex, BMI, ASA, during of operation and duration of anaesthesia (min.). In addition to this, the total lipid profile and renal function test levels were assessed before and after 24h of surgery (Table 1).

Table 2 presents the incidence of nausea, vomiting and PONV among the patients among the group A and group B. Statistically decrease in the incidence of PONV was observed in both groups A and B. A statistically significant decrease was found in the incidence of nausea vomiting PONV in group B in comparison group A. In this comparative study, the incidence of nausea, vomiting and PONV was significantly decreased in patients having fixed dose of granisetron.

The levels of total lipid LDL and TG were found significantly decreased after 24h of surgery ($p < 0.05$) but it was found that

Total number of patients understudy = 40			P
Drugs under study	**Ondansetron (n = 20) (4.0 mg fixed dose)**	**Granisetron (n = 20) (0.75mg fixed dose)**	
Age (years)	48 ± 11	45 ± 14	0.231
Sex (Male/ Female)	06/14	05/15	
Weight (kg)	65.23 ± 12.88	69.42 ± 15.64	0.273
Height (M)	5.71 ± 0.49	5.88 ± 0.68	0.431
BMI (kg/M^2)	23.78 ± 3.21	24.22 ± 4.03	0.122
ASA Class I:II	18:12	21:09	
Smoking habit	05	04	
Motion sickness (History)	06	08	
Total lipid (mg/dL) Before surgery/after surgery	225.05 ± 41.55/197.89 ± 34.74	220 ± 35.41/180 ± 30.55	0.144
LDL(mg/dL) Before surgery/after surgery	114.51 ± 25.65/97.15 ± 24.88	110 ± 22.48/80 ± 21.36	0.156
TG(mg/dL) Before surgery/ after surgery	168.45 ± 29.85/145.84 ± 22.47	162 ± 27.59/154 ± 21.84	0.148
Urea (mg/dL) Before surgery/after surgery	28.75 ± 9.46/32.14 ± 11.65	25.54 ± 8.99/31.25 ± 11.84	0.169
Creatnine(mg/dL) Before surgery/after surgery	0.98 ± 0.25/1.11 ± 0.41	0.84 ± 0.21/1.09 ± 0.41	0.178
During of Operation (Min.)	55.06 ± 16.43	59.17 ± 17.28	0.688
Duration of Anesthesia (Min)	77.12 ± 14. 53	79.42 ± 26.34	0.734
PNOV (History)	One	No	
PNOV (Incidence)	12	08	

Table 1: Demographic profile of patients understudy.

Note: BMI- Body mass index, SD- Standard Deviation, ASA -American society of Anesthesia, Values are mean ± SD or Number of patients (Percentage).

Drugs	Group A (n=20)			Group B (n=20)		
	Nausea (%age)	Vomiting (%age)	PONV (%age)	Nausea (%age)	Vomiting (%age)	PONV (%age)
0h	00	00	01(05.0)	00	00	00
01h	05(25.0)	05(25.0)	04(20.0)	02(10.0)	02(10.0)	03(15.0)
02h	06(30.0)	05(25.0)	06(30.0)	03(15.0)	03(15.0)	02(10.0)
06h	07(35.0)	06(30.0)	07(35.0)	05(25.0)	05(25.0)	06(30.0)
12h	9(45.0)	09(45.0)	08(40.0)	06(30.0)	06(30.0)	05(25.0)
24h	10(50.0)	09(45.0)	10(50.0)	06(30.0)	06(30.0)	06(30.0)

Table 2: Incidence of nausea, vomiting and PONV among the groups.

Note: Values are expressed as number of patients, $p < 0.05$ compared with control.

levels of urea and creatinine were significantly increased. Group B showed a statistically significant lower incidence of nausea vomiting and PONV as compare to ondansetron ($p < 0.05$).

Discussion and Conclusion

The present study was planned to compare to the antiemetic effect of ondansetron and granisetron, and the results of the present study showed a significant decrease in the incidence of nausea vomiting and PONV in group A and B after laparoscopic cholecystectomy under general anaesthesia. However, it was observed in our study that incidence of PONV was even much lower in the patients receiving granisetron, i.e., in group B.

Granisetron decreases antiemetic symptoms in a dose-dependent manner i.e. 20, 40 and 80 microgram/kg of body weight of

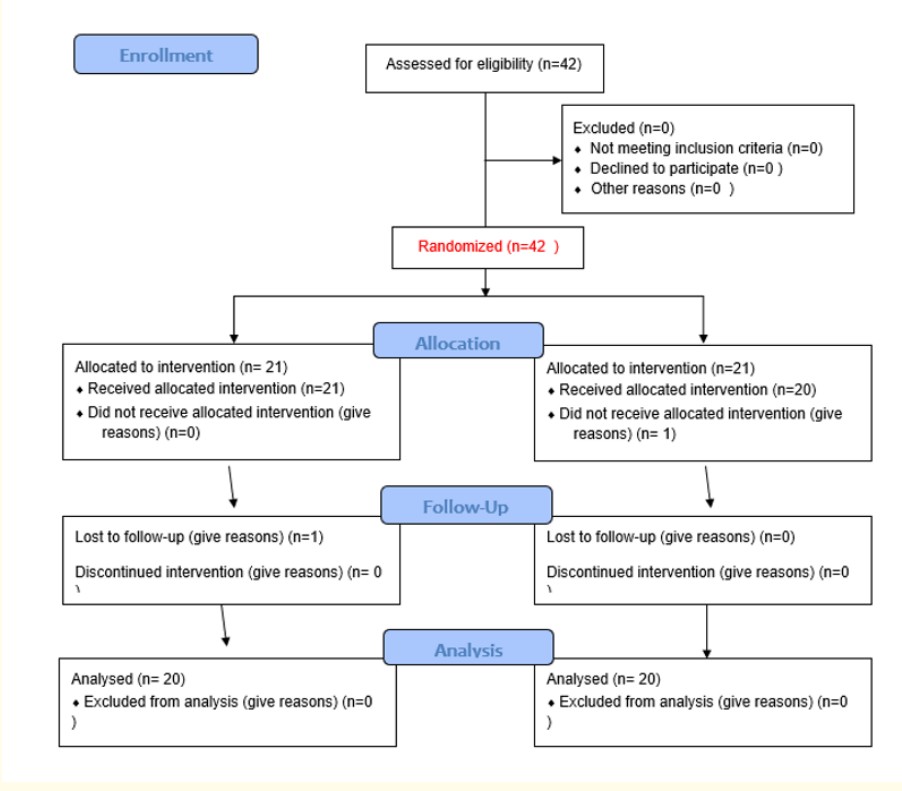

Figure 1

granisetron and also reduces PONV [7]. Researchers reported that ondansetron (4mg) has significantly higher antiemetic symptoms as compare to granisetron [5,6]. They also reported that the anti- emetic symptoms with ondansetron administrated group last for 4-5 h, and these findings were similar to other researcher [6,18].

PONV was found to be 25% with ondansetron and 20% with granisetron where granisetron 1mg and ondansetron 4mg used for modified radical mastectomy which confirms that granisetron is more effective in reducing the incidence of PONV [19]. Similarly, In our study, the overall incidence of PONV was found to be 40% in group A and 30% in group B due to difference in t1/2.

Ondansetron, granisetron, and dexamethasone have decreased PONV in patients undergoing laparoscopic cholecystectomy [9], and the total incidence of PONV was reduced to 35% with ondansetron, 30% with granisetron, and 25% with dexamethasone respectively as compare to 75% with placebo($p < 0.05$) [6,9] and this study supports the finding observed in your study.

In our results, the incidence of nausea vomiting was significantly decreased in patients having fixed dose of granisetron was further supported by other research workers who worked on prevention of PONV with dose variation of granisetron and authors also reported that there was statistically decrease in the incidence of PONV was observed in both ondansetron and granisetron in comparison to control group [20]. These results were found similar to a study with ondansetron (100microgram/kg) and granisetron (40 micrograms/kg) administered intravenously and observed that granisetron significantly decreases the PONV in patients after 6hours of strabismus surgery [21].

We also noted that incidence of vomiting (20%) as compared to nausea (15%) is significantly less in subjects with granisetron ($p > 0.05$) that shows better antiemetic effect than the anti-nausea effect of ondansetron. Also, granisetron shows better anti-nausea (8%) effect than antiemetic effect.

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