ORIGINAL RESEARCH

A study to compare preoperatively palanosetron with ondansetron for postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia

[1]Dr.Shivani Singh, [2]Dr.Namrata Nair, [3]Dr. Ankursahu, [4]Dr. Ratikesh Gupta, [5]Dr. Amanjain, [6]Dr. Radhikakhare

[1,3,4,5]PG Resident, [2]Assistant Professor, L.N Medical College and J.K Hospital, Bhopal, India
[6]Senior Resident, GMC Ratlam, Madhya Pradesh, India

Correspondence Author
Dr. Ratikesh Gupta
PG Resident, L.N Medical College and J.K Hospital, Bhopal, India

Received: 19 June, 2023 Accepted: 19 July, 2023

ABSTRACT

Background: Postoperative nausea and vomiting (PONV) is a common and distressing complication of surgery under general anesthesia. The present study was conducted to compare palanosetron with ondansetron for postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

Material & Methods: The present randomized double blind study was conducted among 80 patients. Using double blind randomization technique, these patients were divided into Group A (Ondansetron 4 mg fixed dose), Group B (Palonosetron 0.075 mg fixed dose). Any incidence of nausea, retching or vomiting and use of any rescue medication during the first 24 h at time were noted. Side effects were registered. Statistical analyses were done using Statistical Package for Social Science Version 9.0 (SPSS LTD, Chicago, IL and U. S. A). A $P < 0.05$ was accepted as statistically significant.

Results: Mean duration of anesthesia in Group A(32.76mins) and group B (33.76mins) shows non-significant difference. Mean duration of intraoperative fentanyl used in Group A (97.6mins) and group B (96.8 mins) shows non-significant difference. Nausea in Group A patients (25%) and group B (15%) shows significant difference. Retching in Group A patients (5%) and group B (2.5%) shows non-significant difference. Vomiting in Group A patients (20%) and group B (10%) shows non-significant difference. Patients requiring rescue antiemetic in Group A patients (32.5%) and group B (15%) shows significant difference. Incidence of total PONV in Group A patients (50%) and group B (27.5%) shows significant difference. Headache in Group A patients (20%) and group B (7.5%) shows significant difference. Diarrhoea in Group A patients (5%) and group B (2.5%) shows non- significant difference. Dizziness in Group A patients (7.5%) and group B (12.5%) shows significant difference.

Conclusion: The present study concluded thatin patients undergoing laproscopic cholecystectomy under general anaesthesia,preoperativelypalanosetron provides a greater anti-nausea impact than preoperativelyondansetron, reduces the need for rescue antiemetics, has a better side effect profile, and has a lower incidence of complete PONV.

Keywords: Laparoscopic cholecystectomy, general anaesthesia, palanosetron, ondansetron,

INTRODUCTION

Postoperative nausea and vomiting is defined as any nausea, retching or vomiting occurring during the first 24 – 48 hours after surgery.[1] Postoperative nausea and vomiting occurs in 20 % to 30 % of patients and are the second among the most common complaints reported, pain being the most common.[2] The incidence of PONV remains unacceptably high (40-75% in the first 24hrs, without active intervention) following laparoscopic cholecystectomy. [3,4] The 5-hydroxytryptamine-3 (5-HT3) receptor antagonists are popular drugs for PONV prophylaxis because of their similar efficacy to droperidol or dexamethasone and their favourable side-effect profile.[5]Ondansetron was one of the first 5-hydroxytryptamine-3 (5-HT3) receptor antagonists to be used in the prophylaxis of postoperative nausea and vomiting (PONV) and, currently, it is still widely used. In the same pharmacological class, palonosetron has a receptor binding affinity 100 times that of other antiemetics.[6] Its use has been reported in the control of

PONV with a prolonged half-life of 40 hours and therapeutic effect lasting up to 72 hours when administered intravenously. Palonosetron is the only 5-HT3 receptor antagonist not associated with prolonged QT interval.[7] Though palonosetron has been extensively used for prevention of chemotherapy induced nausea and vomiting, it has only recently been approved by FDA for use in prophylaxis against PONV. Palanosetron has been compared with placebo for prevention of PONV in patients undergoing open abdominal and gynecological surgeries.[8,9]The present study was conducted to compare palanosetron with ondansetron for postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anaesthesia.

MATERIAL & METHODS

The present randomized double blind study was conducted among 80 patients. Before the commencement of the study ethical clearance was taken from the Ethical Committee of the institute and informed consent was taken from the patients after explaining them the study. Patients between 18–60 years, ASA grade I-II and Apfel score ≥2[10]undergoing elective laparoscopic cholecystectomy under general anaesthesia were included in the study.[10]Patients with known history of allergy to any drug being used in the study, history of vomiting/retching/nausea/antiemetics in 24 h preceding administration of anesthesia, patients on chronic steroids/prokinetics/antiemetics/antacids, menstruating/lactating or pregnant females, h/o alcohol or substance abuse, significant disease of major organs like liver, kidneys, heart, lungs and bone marrow were excluded from the study.Using double blind randomization technique, these patients were divided into Group A (Ondansetron 4 mg fixed dose), Group B (Palonosetron 0.075 mg fixed dose).

INTERVENTIONS

Pre emptively, the group A received 4 mg ondansetron 5 min prior to the induction of general anesthesia. In the group B, 0.075 mgPalonosetronwas administered 5 min prior to the induction of general anesthesia. After preoxygenation, all patients underwent intravenous anesthesia in the following sequence of injections: 0.05 mg/kg midazolam, 2 µg/kg fentanyl, and 2 mg/kg propofol. The airway managed with appropriate sized laryngeal mask airway (LMA). Anesthesia was maintained through the propofol infusion of 50 - 150 µg/kg/h and 0.2 - 0.3 mg/kg atracurium. Mechanical ventilatory support was employed so as to maintain of the end-tidal CO2 pressure (Et CO2) with 35 ± 5 mmHg. The patient monitoring was performed via pulse oximetry, non-invasive blood pressure check, electrocardiography and capnography. Abdominal insufflations with CO_2 were conducted with an intraabdominal pressure less than 14 mmHg. During the surgery, intra abdominal pressure (IAP) of 10–12mm Hg was maintained. At the end of surgical procedure, Ryle's tube was suctioned and removed. Residual neuro muscular blockage was antagonized using i.v.glyccopyrrolate and i.v.neostigmine and trachea was extubated after signs of adequate neuro muscular reversal. For post-operative analgesia, injection diclofenac sodium 1mg/kg intramusculary was administered half an hour before the end of surgery. Intravenous crystalloids were used during intraoperative and immediate post operative period (2 ml/kg/hr). After the surgery, patients were shifted to Post anesthesia care unit and blood pressure, heart rate, respiratory rate and O2 saturation were monitored continuously.Pain intensity was assessed using VAS. Post operative pain relief was provided with injection diclofenac sodium 1mg/kg intramuscularly 8 h. If VAS score was ≥4, rescue analgesia was provided with injparacetamol (1gm) intravenouslyAny incidence of nausea, retching or vomiting and use of any rescue medication during the first 24 h at time interval of 0,1/2, 6,12 and 24 h were noted in the PACU.Retching and vomiting were collectively termed emetic episodes.For the purpose of study, all episodes of nausea which were immediately followed by retching or vomiting were taken as episode of retching or vomiting respectively. In case, the patient exhibited all the three symptoms within 1–2 min, it was taken as one episode of vomiting for statistical purpose. Nausea (>10 min) without retching or vomiting was taken as episode of nausea . Inj dexamethasone 8mg i.v. slowly was given to patients as rescue treatment in the event of patient having nausea lasting more than 10 min duration, or an episode of retching or emesis. Patients who experience PONV despite receiving antiemetics were classified as treatment failure. Side effects registered were headache, diarrhea and dizziness in the initial 24 h.Statistical analyses were done using Statistical Package for Social Science Version 9.0 (SPSS LTD, Chicago, IL and U. S. A). Values were presented as mean with standard deviation or number (%). The data obtained from the study was statistically analyzed among the two groups using the Student t-test and chi square test for multiple comparisons. A $P <$ 0.05 was accepted as statistically significant.

INCLUSION CRITERIA

ASA1 and ASA2 patients.Age 18 -60

EXCLUSION CRITERIA

1. Patient refusal
2. Pregnant females
3. BMI>30 Kg/sq.meter
4. History of cardiovascular, pulmonary , renal and endocrine disease
5. Hemoglobin <10g/dl

RESULTS

In the present study, 80 patients were included andpatients were divided into Group A (Ondansetron 4 mg fixed dose), Group B (Palonosetron 0.075 mg fixed dose).

Table 1: Demographic characteristics of patients

	Group A (n=40)	Group B(n=40)
Mean Age (years)	37.34	35.46
Gender		
Male (%)	19(47.5%)	17(42.5%)
Female(%)	21(52.5%)	23(57.5%)
Mean Weight(Kg)	68.13	67.86
ASA		
ASA I	25	23
ASA II	15	17

Mean age of group A patients were 37.34 years and Group B patients were 35.46 years. Females were more than males in both groups. Mean weight of group A patients were 68.13kg and Group B patients were 67.86kg. In both groups ASA I patients were more than ASA II patients.

Table 2: Perioperative characteristics

Variable	Group A	Group B	P value
Mean duration of anesthesia (min)	32.76	33.76	>0.05
Mean duration of intraoperative fentanyl used (µg)	97.6	96.8	>0.05
Nausea(%)	10(25%)	6(15%)	<0.05
Retching(%)	2(5%)	1(2.5%)	>0.05
Vomiting (%)	8(20%)	4(10%)	>0.05
Patients requiring rescue antiemetic (%)	13(32.5%)	6(15%)	<0.05
Incidence of total PONV (%)	20(50%)	11(27.5%)	<0.05

Mean duration of anesthesia in Group A(32.76mins) and group B (33.76mins) shows non-significant difference. Mean duration of intraoperative fentanyl used in Group A(97.6mins) and group B (96.8 mins) shows non-significant difference. Nausea in Group A patients (25%) and group B (15%) shows significant difference. Retching in Group A patients (5%) and group B (2.5%) shows non-significant difference. Vomiting in Group A patients (20%) and group B (10%) shows non-significant difference. Patients requiring rescue antiemetic in Group A patients (32.5%) and group B (15%) shows significant difference. Incidence of total PONV in Group A patients (50%) and group B (27.5%) shows significant difference.

Table 3: Incidence of side effects

	Group A	Group B	P value
Headache(%)	8(20%)	3(7.5%)	<0.05
Diarrhoea(%)	2(5%)	1(2.5%)	>0.05
Dizziness(%)	3(7.5%)	5(12.5%)	>0.05

Headache in Group A patients (20%) and group B (7.5%) shows significant difference. Diarrhoea in Group A patients (5%) and group B (2.5%) shows non- significant difference. Dizziness in Group A patients (7.5%) and group B (12.5%) shows significant difference.

DISCUSSION

Laparoscopic cholecystectomy is a well-known procedure for treatment of gall stone disease in patients with normal hemoglobin, but in hemoglobinopathic patients, there is still some debate about safety and feasibility of this procedure. Preparation of hemoglobinopathic patients for surgery is quite different: anemia is common because of hemolysis, immunity is compromised and they are liable for vasoocclusive crisis. Due to the improvement in medical care, patients survive to adulthood therefore facing complications of the disease. Optimum preoperative hemoglobin level and necessity for preoperative transfusion to decrease perioperative morbidity and mortality is still a controversial issue and surgeons should be aware about history of previous transfusions which may indicate the possibility of iron deposition sequelae.[11]During initiation of vomiting

reflex there is 5-HT 3 receptor stimulation. [12] The central 5-HT 3 receptors are present in the medullary chemoreceptive trigger zone. Anaesthetic agents activates these receptors. They also act on enterochromaffin cells of the small intestine receptors thereby releasing serotonin which subsequently stimulates 5-HT 3 receptors present on vagus nerve afferents. [13]Mean age of group A patients were 37.34 years and Group B patients were 35.46 years. Females were more than males in both groups. Mean weight of group A patients were 68.13kg and Group B patients were 67.86kg. In both groups ASA I patients were more than ASA II patients.Mean duration of anesthesia in Group A(32.76mins) and group B (33.76mins) shows non-significant difference. Mean duration of intraoperative fentanyl used in Group A (97.6mins) and group B (96.8 mins) shows non-significant difference. Nausea in Group A patients (25%) and group B (15%) shows significant difference. Retching in Group A patients (5%) and group B (2.5%) shows non-significant difference. Vomiting in Group A patients (20%) and group B (10%) shows non-significant difference. Patients requiring rescue antiemetic in Group A patients (32.5%) and group B (15%) shows significant difference. Incidence of total PONV in Group A patients (50%) and group B (27.5%) shows significant difference. Headache in Group A patients (20%) and group B (7.5%) shows significant difference. Diarrhoea in Group A patients (5%) and group B (2.5%) shows non- significant difference. Dizziness in Group A patients (7.5%) and group B (12.5%) shows significant difference.Randeep AM, et al compared the efficacy of palonosetron and ondansetron for prevention of post-operative nausea and vomiting in patients undergoing thyroidectomy under general anaesthesia. From the study they concluded that palonosetron is similar to ondansetron in prevention of postoperative nausea and vomiting in patients undergoing thyroidectomy under general anaesthesia.[14]Laha B et al concluded that Palonosetron is comparable to ondansetron for PONV prophylaxis in elective laparoscopic cholecystectomy when administered as single pre-induction dose.[15]F.J. Davolos, et al tested the hypothesis that, within the margin of 15% of risk difference, palonosetron is not inferior to ondansetron in reducing the incidence of postoperative nausea and vomiting (PONV) in laparoscopic cholecystectomy. A high incidence of PONV was observed at 2---6 hours postoperatively, with a rate of 36.8% (95% confidence interval [CI] 28.2---46.3) in the palonosetron group, as compared to 43.4% (95% CI 34.4---52.9) in the ondansetron group. The risk difference (95% CI) between palonosetron and ondansetron for PONV was 0 (-10.9 to 10.9) at 0---2 hours, -6.6 (-19.4 to 6.5) at 2---6 hours, -0.9 (-11.0 to 9.2) at 6---12 hours, and -2.8 (-9.6 to 3.6) at 12---24 hours. There was no statistically significant difference between the palonosetron and ondansetron groups in the use of rescue medication (dimenhydrinate). There were no adverse events associated with the medications under study.[16]Bhalla J et al concluded that Palanosetron has got better anti-nausea effect, less need of rescue antiemetics, favourable side effect profile and a decrease in the incidence of total PONV as compared to ondansetron in 24 h post operative period in patients undergoing laproscopic cholecystectomy under general anesthesia.[17]

CONCLUSION

The present study concluded thatin patients undergoing laproscopic cholecystectomy under general anaesthesia, preoperativelypalanosetron provides a greater anti-nausea impact than preoperativelyondansetron, reduces the need for rescue antiemetics, has a better side effect profile, and has a lower incidence of complete PONV.

REFERENCES

1. Pierre S, Whelan R. Nausea and vomiting after surgery. Continuing Education in Anaesthesia Critical Care & Pain 2013;13(1):28–32.
2. Apfel CC. Postoperative nausea and vomiting. Miller's anesthesia. 8th edn. Philadelphia: Elsevier Inc 2016:2947-2973.
3. Turkistani A, Abdullah K, Manaa E, Delvi B, Khairy G, Abdulghani B, et al. Effect of fluid preloading on postoperative nausea and vomiting following laparoscopic cholecystectomy. Saudi J Anaesth 2009;3:48-52.
4. Grover VK, Mathew PJ, Hegde H. Efficacy of orally disintegrating ondansetron in preventing postoperative nausea and vomiting after laparoscopic cholecystectomy: A randomised, double-blind placebo controlled study. Anaesthesia 2009;64:595-600.
5. Muchatuta NA, Paech MJ: Management of postoperative nausea and vomiting: focus on palonosetron. TherClin Risk Manag 2009; 5: 21 – 34.
6. Wong EH, Clark R, Leung E, et al. The interaction of RS 25259- 197, a potent and selective antagonist, with 5-HT3 receptors, in vitro. Br J Pharmacol. 1995;114:851---9.
7. Carlisle JB, Stevenson CA. Drugs for preventing postoperative nausea and vomiting. Cochrane Database Syst Rev. 2006:CD004125.
8. Rojas C, Stathis M, Thomas AG, Massuda EB, Alt J, Zhang J, et al. Palonosteron exhibits unique molecular interactions with the 5-HT3 receptor. *AnesthAnalg.* 2008;107:469–78.
9. Muchatuta NA, Paech MJ. Management of postoperative nausea and vomiting: Focus on palanosetron. *TherClin Risk Manag.* 2009;5:21–34.
10. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. *Anesthesiology.* 1999;91:693–700.
11. Mohammed R, Al-Ibadi HF, Redha AG. Perioperative Events of Laparoscopic Cholecystectomy in Patients

with Hemoglobinopathies. The Medical Journal of Basrah University. 2020 Jun 1;38(1):80-8.
12. Bunce KT, Tyers MB. The Role of 5-HT in Postoperative Nausea and Vomiting. Br J Anaesth. 1992;69(supp11):60S–2S.
13. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiol. 1992;77:162–84.
14. Randeep AM, Sunilkumar TS, Beegum TSS, et al. A comparative study of palonosetron and ondansetron for prevention of post-operative nausea and vomiting in patients undergoing thyroidectomy held at central Kerala. J Evid Based Med Healthc 2021;8(42):3596-3601. DOI: 10.18410/jebmh/2021/651
15. Laha B, Hazra A, Mallick S. Evaluation of antiemetic effect of intravenous palonosetron versus intravenous ondansetron in laparoscopic cholecystectomy: a randomized controlled trial. Indian journal of pharmacology. 2013 Jan;45(1):24.
16. F.J. Davolos, N.S. Modolo, L.G. Braz et al., Palonosetron versus ondansetron for prophylaxis of postoperative nausea and vomiting in laparoscopic cholecystectomy: a non-inferiority randomized controlled trial, Brazilian Journal of Anesthesiology, https://doi.org/10.1016/j.bjane.2021.06.020
17. Bhalla J, Baduni N, Bansal P. Comparison of palanosetron with ondansetron for postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy under general anesthesia. J Minim Access Surg. 2015 Jul-Sep;11(3):193-7. doi: 10.4103/0972-9941.140219. PMID: 26195878; PMCID: PMC4499925.