Available online at www.iponlinejournal.com

Journal homepage: www.innovativepublication.com/journal/ijca

Original Research Article

Ramosetron versus Palonosetron in preventing postoperative nausea and vomiting in laparoscopic surgeries

Suma K.V[1], Santhosh K. Gouroji[2*], Gangadhar Meti[3]

[1]Associate Professor, [2]Assistant Professor, [3]Post Graduate, Dept. of Anaesthesiology, JJM Medical College, Davanagere, Karnataka, India

Article Info

Received: 8th July, 2019

Accepted: 22nd July, 2019

Published Online: 22nd August, 2019

Keywords: Laparoscopic surgery, Nausea, Palonosetron, Ramosetron, Retching, Vomiting.

Abstract

Introduction: The incidence of postoperative nausea and vomiting (PONV) following laparoscopic surgeries is very high without antiemetic prophylaxis. $5HT_3$ receptor antagonists are the most commonly used drug for prevention of PONV.

Aims: To compare the effectiveness of intravenous (IV) palonosetron versus ramosetron in prevention of PONV during the 24 hour period in patients undergoing laparoscopic surgeries.

Materials and Methods: Sixty patients enrolled for the study were randomly allotted into two groups of thirty each. Group I received 0.075 mg of IV Palonosetron and Group II received 0.3 mg of IV Ramosetron two minutes before induction of anaesthesia. Both the Groups were similar with respect to age, sex, duration and types of surgery and anaesthetic management. Patients were assessed for the incidence of nausea, retching, vomiting, need for rescue antiemetic and adverse effects at 0-2 hour and 2-24 hours interval following surgery. Students 't' test and chi-square test were used for comparing the parameters. A p-value <0.05 was considered significant.

Results: There was no significant difference between the groups with respect to incidence of nausea, retching and vomiting. The incidence of nausea in group I at 0-2 hours was 3.3% and 6.7% in Group II without a statistically significant difference (p=0.5) and at 2-24 hour interval Group I had 3.3% while Group II had 10% incidence of vomiting with p=0.3 and statistically non-significant. There was no significant difference with respect to incidence of retching, vomiting, need for rescue antiemetic and adverse effects between the two groups.

Conclusion: Both palonosetron and ramosetron are equally effective in prevention of PONV in laparoscopic surgeries.

Introduction

Nausea and vomiting in the period following surgery commonly known as post operative nausea and vomiting (PONV) is a little problem but with increase in the number of day care anaesthesia procedures being done, this little problem has become a big problem.[1] The number of patients complaining of PONV is as high as 80%.[2] It is one of the causes of delayed discharge from the hospital. It also causes patient dissatisfaction, dehydration, electrolyte imbalance, higher pain perception and wound dehiscence in the postoperative period.[3,4]

Numerous patient and surgical factors are responsible for PONV.[5,6] Serotonin release from the enterochromaffin cells by anaesthetic drugs[7] and creation of pneumoperitoneum during laparoscopy stretches the mechanoreceptors resulting in increased serotonin synthesis and PONV.[8] Antihistamines, benzamides and anticholinergics were used to treat PONV after laparoscopic surgery but adverse effects like dryness of mouth, sedation and hypotension were common.[9] $5HT_3$ receptor antagonists that are selective and produce less side effects are better for preventing and treating PONV.[10] Ondansetron along with granisetron were the $5HT_3$ receptor antagonists used first. Ramosetron is a newly developed selective $5HT_3$ receptor antagonist, binds with more affinity to $5HT_3$ receptors and dissociates slower[9] and has longer duration of than ondansetron and granisetron.[10] Palonosetron a second generation $5HT_3$ receptor antagonist was introduced to the market and approved by the Drugs Controller General of India on 25-4-2009. Higher binding affinity to $5HT_3$ receptors, with a longer elimination half life of around 40 hours after a single intravenous dose is seen.[9,11] Many studies have been undertaken in order to compare the effectiveness of ramosetron and palonosetron for prevention of PONV in laparoscopic surgeries. The results are inconclusive with some showing palonosetron to be better,[12] while some showing ramosetron to be better[13] and most of them finding no difference between the two. Therefore this study was done to compare ramosetron and palonosetron in reducing the incidence of postoperative nausea and vomiting (PONV) in laparoscopic surgeries.

*Corresponding Author: Santhosh K. Gouroji, Assistant Professor, Dept. of Anaesthesiology, JJM Medical College, Davanagere, Karnataka, India
Email: santug16@gmail.com
http://doi.org/ 10.18231/j.ijca.2019.082

Materials and Methods

ASA grade I & II patients, 60 in number, scheduled to undergo laparoscopic surgeries electively, both males and females 18 to 60 years of age under general anaesthesia were included in the study. Informed written consent from the patients and institutional ethical committee approval were obtained. Patients with gastrointestinal disorders, advanced liver disease, cardiovascular disorders, morbid obesity, history of drug allergy and antiemetic use in 24 hours before surgery were excluded from the study.

30 patients were randomly allotted in each group.

1. In Group I 0.075 mg intravenous (IV) Palonosetron. was administered
2. In Group II 0.3 mg intravenous (IV) Ramosetron was administered.

A preoperative evaluation and routine laboratory investigations which included complete hemogram, blood urea and serum creatinine, blood sugars, electrocardiogram, bleeding time and clotting time were done on the day prior to the scheduled surgery. Tablet Alprazolam 0.5 mg and tablet Ranitidine 150mg was given the night prior to surgery and were kept nil by mouth from 10 PM onwards. On shifting to the operating table, IV line was secured and 5% Dextrose normal saline was started. Non-invasive blood pressure {NIBP}, SPO2 monitor and ECG were connected. Basal readings were recorded. The study drugs were given by intravenous route two minutes before induction of anaesthesia. Induction of anesthesia was done with injection propofol 2mg/kg IV and injection succinylcholine 2mg/kg IV was administered for muscle relaxation and patients were intubated with appropriate sized cuffed endotracheal tubes. Injection fentanyl 2µg/kg IV was used for analgesia and injection vecuronium 0.05mg/kg IV was used for maintenance of muscle relaxation during surgery. Nitrous oxide (66%) and oxygen (33%) with isoflurane 1% along with intermittent positive pressure ventilation was used for maintenance of anaesthesia. Continuous ECG, pulse oximetry and NIBP were monitored every 5th minute during the intra operative period. Glycopyrrolate 0.008mg/kg IV and neostigmine 0.05 mg/kg IV was administered for reversing the neuromuscular block and extubation was done after meeting the extubation criteria and shifted to recovery room. On meeting the Aldrette score of nine or above patients were shifted from the recovery room.

Patients were observed for postoperative nausea, retching and vomiting during the 24 hours following surgery, at 0-2 hours and 2-24 hours. Spontaneous complaints from the patient or by questioning the patient about the same was used for assessment.

1. Patients expelling gastric contents forcefully from the mouth was considered as vomiting.
2. Patients trying to vomit with a feeling that was unpleasant was considered as nausea.
3. Patients having contraction of the respiratory muscles in a laboured manner that was rhythmic, with spasm and without the gastric contents being expelled was considered as retching.

The necessity for rescue antiemetic was noted and injection ondansetron 4mg IV, was given if the patient had episodes of vomiting during the postoperative period if felt necessary by the observer. Patients were asked about Headache and dizziness. Data obtained was analyzed and comparison done between the two groups. Data was analyzed using SPSS for windows, SPSS Inc. New York. Mean ± SD was used for calculating continuous measurement and categorical measurement results were presented in number (%) and 5% level is considered significant. Student 't' test (two tailed independent) was used for comparison of continuous scale parameters and chi-square / Fisher exact test for comparing parameters on categorical scale between the two groups. A p-value <0.05 is considered significant while <0.01 is strongly significant.

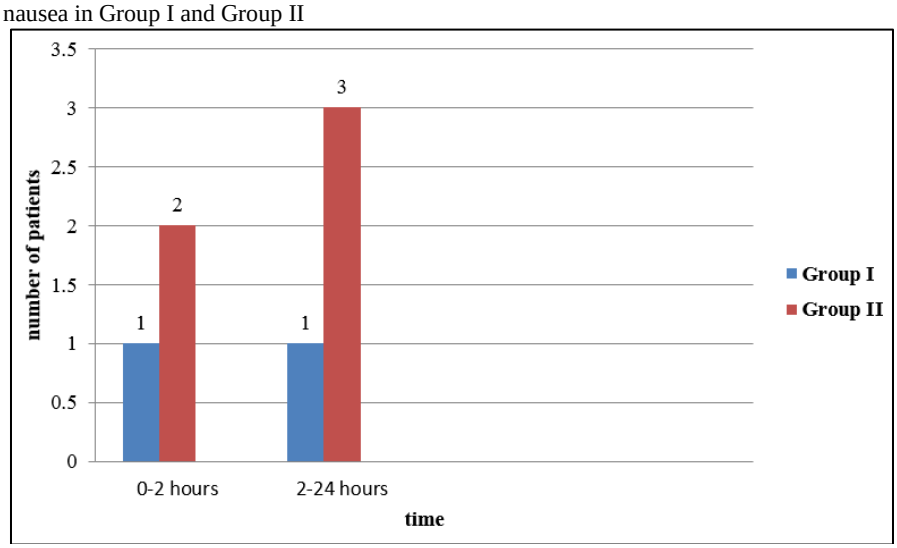
Table 1: Age, sex, weight of patients and duration of surgery

Parameter	Group I		Group II		p-value
Mean age	32.7		37.43		0.179
Weight in kilograms	**Male**	**Female**	**Male**	**Female**	0.184
	61.47	52.6	59.2	54.2	
Sex of patients	**Male**	**Female**	**Male**	**Female**	0.436
	15	15	12	18	
Mean duration of surgery in minutes	70.83		81.90		0.118

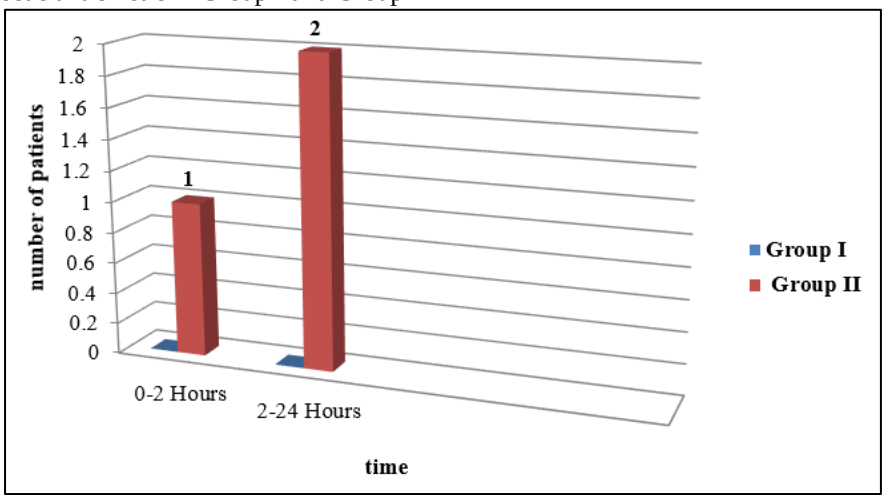
Table 2: Incidence of nausea, retching, vomiting, need for rescue antiemetic and adverse effects

Parameter		Group I	Group II	p-value
Nausea	0-2 hours	1 (3.3%)	2 (6.7%)	0.554
	2-24 hours	1 (3.3%)	3 (10%)	0.306
Retching	0-2 hours	0	0	-
	2-24 hours	0	1 (3.3%)	0.313
Vomiting	0-2 hours	0	2 (6.7%)	0.15
	2-24 hours	0	2 (6.7%)	0.15
Need for rescue antiemetic	0-2 hours	0	1 (3.3%)	0.313
	2-24 hours	0	2 (6.7%)	0.15
Adverse effects	Headache	0	1 (3.3%)	0.3
	Dizziness	0	1 (3.3%)	0.3

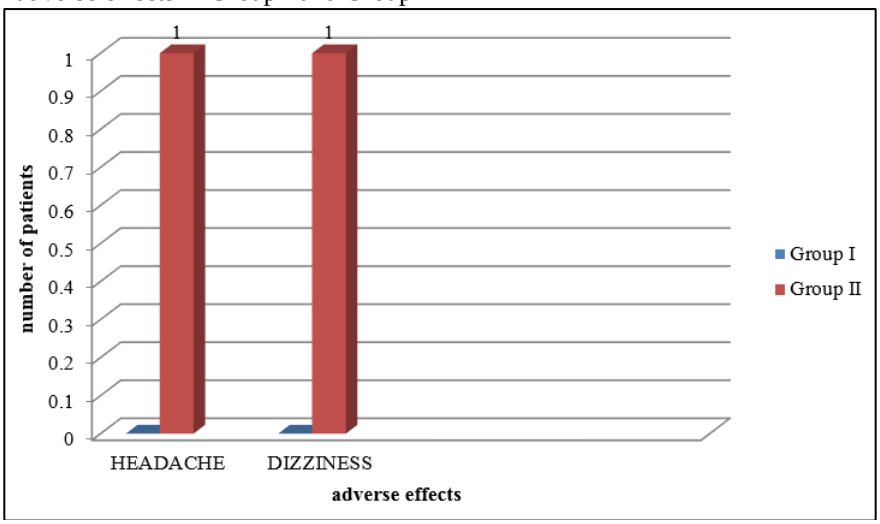
Graph 1: Incidence of nausea in Group I and Group II



Graph 2: Need for rescue antiemetic in Group I and Group II



Graph 3: Incidence of adverse effects in Group I and Group II



Results

Study was completed by all the patients. Age, weight, sex, type of surgery and duration of surgery was same in both groups. During the 0-2 hour interval single patient (3.3%) in group I and two patients (6.7%) in group II had complaints of nausea and was statistically non significant (p=0.55). In the 2-24 hours interval one patient (3.3%) in group I and three patients (10%) in group II had a sensation of nausea which was statistically non significant (p=0.30).

No patients in either group I or group II had complaints of complaints of retching in the 0-2 hour period. In the 2-24 hours interval, not even a single patient in group I and single patient (3.3%) in group II complained of retching and was statistically non significant (p=0.313). In group I no patient had vomiting while two patients (6.7%) in group II had vomiting during the 0-2 hour interval and was statistically non significant (p=0.15). During the 2-24 hour interval no patient in group I and two patients (6.7%) in group II had vomiting and was statistically non significant (p=0.15). Out of two patients who complained postoperative nausea in group I none of them received rescue antiemetic while out of five patients who complained of vomiting, retching or nausea in group II, three patients received rescue antiemetic (one during the 0-2 hour interval and two during the 2-24 hour interval) and was statistically non significant (p=0.56). Headache or dizziness was not seen in any patients in group I and one patient in group II complained of headache and one patient complained of dizziness and was statistically non significant (p=0.3).

Discussion

Pain and emesis are the commonly encountered complaints after anaesthesia and surgery. Patient distress and even delayed discharge from the hospital is caused by nausea and vomiting.[14] The incidence of PONV on an average is between 20% to 30%[15] but can be very high upto 72% after laparoscopic cholecystectomy[8] and up to 80% in gynecological laparoscopic surgeries.[9] PONV has a multifactorial causes like age, sex, smoking, duration and type of surgery, intra operative use of opioid and inhalation agents.[8,14]

$5HT_3$ receptors stimulation in the chemoreceptor trigger zone caused by the anaesthetic agents, intestinal ischemia due to pneumoperitoneum and subsequent serotonin release and mechanoreceptors mediated stimulation of the gut due to creation of pneumoperitoneum results in an increased incidence of PONV.[8,15] Ramosetron which is a $5HT_3$ receptor antagonists and used in cisplatin induced emesis because of its high potency and bio-availability has been found to be very effective. It acts by exerting its effects on area postrema and nucleus tractus solitaries both of which are rich in $5HT_3$ receptors.[12,16] Palanosetron which is a second generation $5HT_3$ receptor antagonist exhibits allosteric action on $5HT_3$ receptors. This allosteric binding with resultant change in the conformation of the serotonin receptor indirectly inhibits the serotonin binding. As a result palonosetron has a higher affinity to $5HT_3$ receptors and this leads to a greater potency and prolonged duration of action compared with other $5HT_3$ receptor antagonists.[17]

The effective dose of ramosetron needed to prevent of PONV was 0.3mg according to Fuji et al in patients being operated for gynecological surgery.[18] The dose recommended by the manufacturer is also 0.3mg once in a day. Therefore we used the same dose of ramosetron in our study. Kovac LA and colleague in their study performed in patients undergoing major gynecological and laparoscopic surgery used 25µg, 50µg and 75µg of palonosetron in prevention of PONV and concluded 75µg of palonosetron to be most effective and safe.[19] Hence we chose 75µg of palonosetron for this study. We did not consider a placebo group in our study because Aspinall and Goodman were of the view that we should not have a placebo group when effective drugs are present for prevention of PONV, which has high incidence after laparoscopic surgery.[20] We used a oral questionnaire for the assessment of complaints of nausea, retching and vomiting as most of our patients were uneducated.

An incidence of 3.3% nausea was found in palonosetron group during 0-2 hour period (1 out of 30 patients) and in the ramosetron group was 6.7% (2 out of 30 patients) and at 2-24 hours period 3.3% (1 out of 30 patients) reported nausea in the palonosetron group and 10% (3 out of 30 patients) in the ramosetron group. In the 0-2 hour period vomiting was not seen in any patients in palonosetron group and seen in 6.7% in ramosetron group. At 2-24 hours, vomiting was not observed in any patients in palonosetron group and observed in 6.7% in ramosetron group.

In a study by Gautam Piplai et al[12] to compare the effects of ramosetron and palonosetron in prevention of PONV in patients posted for laparoscopic cholecystectomy the number of patients complaining of nausea and vomiting in the 0-48 hour period was same in both the groups correlates to our study. However the number of patients with PONV over 48-72 hours period was found to be significantly less in the palonosetron group. Sarbari Swaika et al[13] in their study on patients operated for laparoscopic cholecystectomy, reported ramosetron better and alternative choice than palonosetron in reducing PONV incidence in the early (0-2 hour) postoperative period and is not same as our findings, During the 6-24 hour interval no statistically significant difference was seen between the two drugs and is same as our findings.

Won-Suk Lee,[9] in patients scheduled to undergo laparoscopic hysterectomy, found that the number of patients having PONV was same in the palonosetron, granisetron and ramosetron at 0-6 and 6-24 hour period and corresponds to our results.. The findings of this study correlate to those observed by Soo Kyoung Park et al[21] who concluded that no significant difference was present between palonosetron and ramosetron in PONV prevention in patients who underwent gynecological laparoscopic procedures. In a metaanalysis involving seven studies done Min Soo Kim et al[11] in order to compare palonosetron and ramosetron for the prevention of PONV no difference was

observed between the two drugs that corresponds to our finding. Chattopadhay Suman et al[22] in their study done on patients posted for caesarean section under spinal found palonosetron produced less PONV than ramosetron in the 48 hour period after surgery, the results of which do not correspond to our findings.

Patients with a requirement of rescue antiemetic was higher in ramosetron group 10% compared to 0% in palonosetron group (p=0.56) but was not statistically significant and is similar to the results obtained by Firdous Ahmed Yatoo et al[15] and Won Suck Lee et al.[9] Headache and dizziness were seen in 0% in palonosetron and 6% in ramosetron p=013 and was similar to the studies conducted by Won Suck Lee et al[9] and Gautam Piplai et al.[12]

Conclusion

In conclusion PONV incidence in palonosetron group was less compared to ramosetron group, but was statistically non significant. Hence there is not much difference between the two drugs in preventing PONV after laparoscopic surgeries. However studies are needed.

Conflict of Interest: None.

Source of Funding: None.

References

1. Kapur PA. The big "little problem". *Anest Analg* 1991;73:243-5.
2. Ahn E, Choi G, Kang H, Baekm C. Palonosetron and ramosetron compared for effectiveness in preventing postoperative nausea and vomiting; A systematic review and meta analysis. PLOS ONE\Journal.Pone.0168509.
3. Sebastin Pierre, Rachel Whelan. Nausea and vomiting after surgery. Continuing Education in Anaesthesia. *Critical Care Pain* 2013;13.
4. Bhattacharya D, Dey, Satarjit D, Nayak S, Roy P, Acharya A et al. A comparative study between palonosetron and granisetron to prevent postoperative nausea and vomiting after laparoscopic cholecystectomy. *J Anaesth Clin Pharmacol* 2010;26:480-3.
5. Watcha MF, White PF. Postoperative nausea and vomiting its etiology, prevention and treatment. *Anaesthesiol* 1992;77:162-84.
6. Naylor RJ, Inall FC. The physiology and pharmacology of postoperative nausea and vomiting. *Anaesth* 1994;49(2):5.
7. Lerman J. Surgical and patient factors involved in postoperative nausea and vomiting. *Br J Anesth* 1992;69(1):24-32.
8. Sumyendu G, Anirban P, Amith A, Chaitali B, Tirtha RG, Subhrata G. Palonosetron and palonosetron plus dexamethasone to prevent postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: a prospective, randomized, double- blind comparative study. *Anaesth: Essays Res* 2011;5(2):134-7.
9. Lee WS, Beom K, Lim S, Chang Y. Comparison of palonosetron, granisetron and ramosetron for the prevention of postoperative nausea and vomiting after laparoscopic gynecological surgery: A prospective randomized trial. *BMC Anesthesiol* 2015;15:121.
10. Kim MS, Park JH, Choi YS, Park SH. Efficacy of palonosetron vs. ramosetron for the prevention of postoperative nausea and vomiting: A meta-analysis of randomized control trials. *Yonesi Med J* 2017;58(4)848-58.
11. Baisakhi Laha, Avijit Hazra, S. Mallick. Evaluation of antiemitic effects of intravenous palonosetron versus intravenous ondansetron in laparoscopic cholecystectomy. *Indian J Pharmacol* 2013;45(1).
12. Piplai G, Chakrabarthy I, Mukhopadhyay M, Karmar M, Sarkar S, Bhattachrajee D. A comparative study between palonosetron and ramosteron to prevent postoperative nausea and vomiting after laparoscopic cholecystectomy. *Int Res J Pharm Pharmacol* 2012;2(8):193-7.
13. Swaika S, Pal A, Chatterjee S, Saha D, Dawar N. Ondansetron, ramosetron or palonoseron: Which is a better choice to prevent postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy? *Anesth Essays Res* 2011;5(2):182-6.
14. Saeeda Islam, P.N. Jain. Postoperative nausea and vomiting a review article. *Indian J Anaesth* 48(4):253-8.
15. Firdous Ahmad Yatoo, Kulbhushan Mahotara, Nandita Mehta, Kuldip Gupta. A comparitive study of granisetron, ramosetron, and palonosetron as antiemitics in prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgeries. *J Evol Med Dent Sci* 2016;05(23).
16. Noda K, Ikeda M, Yoshida O, Taguchi T, Shimoyama T. Clinical evaluation of ramosetron against the nausea and vomiting induced by anticancer drugs. *Jpn J Clin Exp Med* 1994;71:2765-76.
17. Y.E. Moon, J. Joo, J.E. Kim and Lee. Antiemitic effect of ondansetron and palonosetron in thyroidectomy: a prospective, randomized, double-blind study. *Br J Anaesth* 2012;108(3):417-22.
18. Fuji Y, Sitoh Y, Tanaka H, Toyooka H. Comparison of ramosetron and granisetron for preventing postoperative nausea and vomiting after gynecologic surgery. *Anesth Anal* 1999;89(2)476-9.
19. Kovac AL, Ebehart L, Kotarski L, Clerici G, Afpel C. A randomized double blind study to evaluate the safety and efficacy of three different doses of palonosetron versus placebo for preventing postoperative nausea and vomiting over a 72 hour period. *Anesth Analg* 2008;107:439-44.
20. Aspinall RL, Goodman NW, Denial of effective treatment and poor quality of information in placebo controlled clinical trials of ondansetron for postoperative nausea and vomiting. A review of published trials. *BMJ* 1995;11:844-6.
21. Park SK, Cho EJ, Kang SH, Lee YJ, Dal-Ah Kim. A randomized, double-blind study to evaluate the efficacy of ramosetron and palonosetron for prevention of postoperative nausea and vomiting after gynecological laparoscopic surgery. *Korean J Anesthesiol* 2013;64(2):133-7.
22. Chattopadhay Suman, Goswami Sebanti. Palonosetron versus ramosetron prophylaxis for control of postoperative nausea and vomiting after cesarean delivery under spinal anesthesia. *J Obstet Gynecol India* 2015;65(1):28-33.

How to cite this article: Suma KV, Gouroji SK, Meti G. Ramosetron versus Palonosetron in preventing postoperative nausea and vomiting in laparoscopic surgeries. *Indian J Clin Anaesth* 2019;6(3):425-9.