10.5005/jp-journals-10050-10078

ORIGINAL ARTICLE

A Clinical Comparative Study of Ondansetron, Palonosetron, Ramosetron, and Metoclopramide for Prevention of Postoperative Nausea and Vomiting in Patients undergoing Laparoscopic and ENT Surgery under General Anesthesia

[1]Vartika Vinay, [2]Anil P Agrawal, [3]AP Verma, [4]Gopal Krishan, [5]Reehan Ahmad, [6]Siddhartha Hanjura

ABSTRACT

Introduction: Postoperative nausea and vomiting (PONV) is a well-known entity following surgical procedures and may result in serious complications including aspiration of gastric contents, prolonged recovery period, and impaired surgical wound healing. Laparoscopic surgery is a known risk factor for PONV. Also, the incidence of vomiting after ear nose throat (ENT) surgeries is relatively high.

Aims and Objectives: Our aim of the study is to compare the effectiveness of ondansetron, palonosetron, ramosetron, and metoclopramide to prevent PONV in patients undergoing laparoscopic and ENT surgery under general anesthesia.

Materials and methods: The present study was conducted on 120 adult patients scheduled for elective laparoscopic cholecystectomy and ENT surgery under general anesthesia. All patients were randomized into four groups (O, P, R, and M) with 30 patients each and received injection ondansetron (4 mg), palonosetron (0.075 mg), ramosetron (0.3 mg), and metoclopramide (10 mg) intravenously during premedication. Patients were observed intraoperatively and 24 hours postoperatively for any episodes of nausea and vomiting. All the patients were observed for side effects, such as dizziness, headache, allergic reactions, etc.

Conclusion: Palonosetron is quite effective in prevention of PONV compared with ramosetron, ondansetron, and metoclopramide given intravenously for various surgical procedures under general anesthesia. Its effectiveness in PONV provides a new cost-effective agent to the present recital of antiemetic drugs.

Keywords: Laparoscopic and ENT surgery, Metoclopramide, Ondansetron, Palonosetron, Postoperative nausea and vomiting, Ramosetron.

How to cite this article: Vinay V, Agrawal AP, Verma AP, Krishan G, Ahmad R, Hanjura S. A Clinical Comparative Study of Ondansetron, Palonosetron, Ramosetron, and Metoclopramide for Prevention of Postoperative Nausea and Vomiting in Patients undergoing Laparoscopic and ENT Surgery under General Anesthesia. Int J Adv Integ Med Sci 2017;2(2):65-69.

Source of support: Nil

Conflict of interest: None

[1,5,6]Junior Resident (3rd Year), [2]Associate Professor, [3]Professor [4]Assistant Professor

[1,3-6]Department of Anesthesiology, Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India

[2]Department of Orthopedics, Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India

Corresponding Author: Vartika Vinay, Junior Resident (3rd Year), Department of Anesthesiology, Rohilkhand Medical College & Hospital, Bareilly, Uttar Pradesh, India, Phone: +917500308024, e-mail: drvartikavinay@gmail.com

INTRODUCTION

Postoperative nausea and vomiting (PONV) is defined as any nausea, retching, or vomiting occurring during the first 24 to 48 hours after surgery in patients. The PONV may take place in single or multiple episodes, which may last for minutes, hours, or even days.[1] The PONV is one of the most common causes of patient dissatisfaction after anesthesia, with reported incidences of 30% in all postsurgical patients and a relatively high incidence (60–80%) after middle ear surgery.[2] The ear nose throat (ENT) surgeries have a high incidence of postoperative emesis when no prophylaxis is done.[3,4] Laparoscopic surgery has decreased the morbidity associated with cholecystectomy, but PONV is the commonly observed adverse effect after general anesthesia in these patients, and its incidence ranges between 60 and 72%.

The etiology of PONV is multifactorial. Koivuranta et al identified five risk factors, namely female gender, nonsmoking status, history of PONV, history of motion sickness, and duration of surgery >60 minutes. Incidence of PONV increases with every risk factor.[5]

Use of opioid analgesics usually causes PONV. Antiemetics are used liberally with the use of opioids. The emetogenic effect of inhalational anesthetics and opioids appears to be dose related. Longer procedures, with concomitantly longer anesthesia times and increased postoperative opioid consumption, are associated with an increased incidence of PONV.

Emetogenic drugs commonly used in anesthesia include nitrous oxide, neostigmine, and opioids.[6] Most of the research on PONV and efficacy of antiemetics has been with general anesthesia, while PONV is a distressing problem in regional anesthesia too; however, use of regional anesthesia is associated with a lower incidence

of PONV than general anesthesia in both children and adults.[7]

Ondansetron was the first commercially available 5-hydroxytryptamine (5-HT_3) receptor antagonist. This class of antiemetics exhibits minimum side effects with good clinical results. It selectively blocks serotonin 5-HT_3 receptors, with little or no effect on dopamine receptor.

Palonosetron is a new 5-HT_3 receptor antagonist that can be distinguished from older 5-HT_3 receptor antagonists (ondansetron, dolasetron, and granisetron) by its unique chemical structure, greater binding affinity, and considerably longer half-life of 40 hours.[8,9] Palonosetron is proven to be effective in early PONV and in delayed PONV.[10] It is also used in cancer chemotherapy-induced nausea and vomiting.

Ramosetron is a recent 5-HT_3 receptor antagonist, earlier available only in Southeast Asian countries and now worldwide. It has higher affinity for the 5-HT_3 receptor than the older 5-HT_3 antagonists and maintains its effects over 2 days; it is, therefore, significantly more effective for delayed PONV. In recent studies, ramosetron is also effective against irritable bowel syndrome-like symptoms.

Metoclopramide is a benzamide derivative extensively used as an antiemetic. It is a prokinetic drug, which promotes gastric emptying prior to anesthesia and reduces PONV. It also acts by increasing the tone of the lower esophageal sphincter.

Thus, considering the availability of a number of drugs belonging to different categories, we chose to carry out a study to find out the most appropriate drug for PONV in patients undergoing surgery (ENT and laparoscopic cholecystectomy) under general anesthesia.

AIMS AND OBJECTIVES

- To evaluate and compare the clinical efficacy of ondansetron, palonosetron, ramosetron, and metoclopramide as antiemetic intraoperatively and for 24 hours after surgery
- To evaluate the effect of ondansetron, palonosetron, ramosetron, and metoclopramide on hemodynamic parameters intraoperatively and for 24 hours after surgery
- To evaluate requirement of rescue antiemetic
- To evaluate any side effect of ondansetron, palonosetron, ramosetron, and metoclopramide

MATERIALS AND METHODS

The present prospective, randomized, double-blind comparative study was conducted at Rohilkhand Medical College & Hospital, Bareilly, India, between November 2014 and April 2016 on 120 adult patients of American Society of Anesthesiologists physical status I and II scheduled for elective laparoscopic cholecystectomy and ENT surgery under general anesthesia. Randomization was done by computer-generated numbers. The study was approved by the institutional ethical committee, and written informed consent was obtained from all the patients.

All the patients underwent preanesthetic checkup before enrollment for the present study.

Patients were randomly divided into four groups (M, O, P, and R) of 30 patients each.

Patients were preoxygenated with 100% O_2 for 3 minutes. Then, patients were premedicated with intravenous (IV) ranitidine (50 mg), IV butorphanol (1 mg), IV midazolam (1 mg), and IV glycopyrrolate (0.2 mg) and then administered intravenously with one of the test drugs (ondansetron, palonosetron, ramosetron, or metoclopramide in the dose of 4, 0.075, 0.3, and 10 mg respectively) by a person not involved in the study. Then, the patient was induced with injection propofol 2 mg/kg body weight and endotracheal intubation was facilitated with injection succinylcholine 1.5 mg/kg. Maintenance of anesthesia was done with nitrous oxide (67%) and oxygen (33%) and isoflurane (0.6–0.8%) and injection vecuronium. The patient was monitored during anesthesia using continuous electrocardiogram, heart rate, blood pressure, and pulse oximetry. On completion of surgery, the neuromuscular block was reversed with injection neostigmine 0.04 mg/kg and injection glycopyrrolate 0.01 mg/kg. Injection diclofenac, 75 mg intramuscularly was given for postoperative analgesia.

Complete response: No nausea/vomiting episode.

Partial response: One episode of nausea/vomiting or both.

Treatment failure: Two or more episodes of nausea/vomiting or the receipt of a rescue antiemetic.

Rescue antiemetic was an antiemetic drug other than the drug given to the patient of a particular group, which was easily available in the hospital.

The side effects of the study drug like headache, dizziness, allergic reaction, etc., if any, were assessed and recorded. The duration after which the rescue antiemetic given was also recorded for each group.

RESULTS

The patients in all the four groups were statistically comparable with respect to age, sex distribution, mean weight, and mean height, with p value more than 0.005 (Table 1).

As seen in Table 2 and Graph 1, out of 120 patients in the study, a total of 42 patients (35%) were completely relieved of PONV and did not require any rescue antiemetic for first 24 hours postoperatively. Majority of these patients belonged to group P (25 out of 42), with no

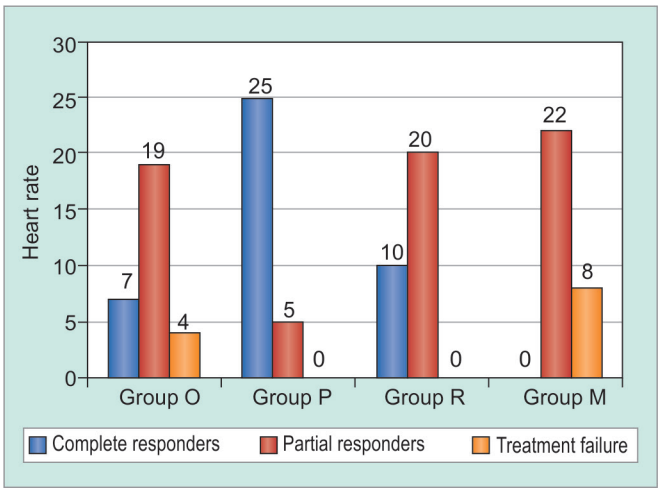
Table 1: Age, sex distribution, mean weight, and mean height of the patients

	Group O	*Group P*	*Group R*	*Group M*	*F-value*	*p-value*
Age (mean ± SD)	34.37 ± 10.4 years	35.5 ± 11.22 years	36.33 ± 10.54 years	34.63 ± 12.09 years	0.195	0.900 (NS)
Sex						
Male	20	24	22	22	1.364	0.713 (NS)
Female	10	6	8	8		
Total	30	30	30	30		
Weight (mean ± SD)	59.07 ± 5.88 kg	58.63 ± 9.99 kg	58.57 ± 9.15 kg	58.1 ± 5.71 kg	0.075	0.973 (NS)
Height (mean ± SD)	159.2 ± 7.2 cm	155.53 ± 8.28 cm	157.83 ± 6.84 cm	157.7 ± 5.52 cm	1.394	0.248 (NS)

SD: Standard deviation; NS: Nonsignificant

Table 2: Response of the patients to given antiemetic

Groups	*Complete responders (%)*	*Partial responders (%)*	*Treatment failure (%)*
O	7 (23.3)	19 (63.3)	4 (13.3)
P	25 (83.3)	5 (16.7)	0 (0)
R	10 (33.3)	20 (66.7)	0 (0)
M	0 (0)	22 (73.3)	8 (26.7)
Total	42 (35%)	66 (55%)	12 (10%)



Graph 1: Response of patients to given antiemetic

patients in group M. The maximum number of patients (55%) out of the total patients came out as partial responders, experiencing single episode of PONV in the postoperative period. Rest 10% of patients were categorized as treatment failure, i.e., they required two or more doses of rescue antiemetic postoperatively. None of the patients in group P or R came out as treatment failures, whereas four patients in group O and eight patients in group M were included in treatment failure.

The incidence of nausea and vomiting was noted in each group (Table 3 and Graph 2). The total episodes of nausea in groups O, P, R, and M were 18, 4, 13, and 24 respectively. As evident, the maximum episodes occurred in group M (80%) and minimum in group P (4%). The statistics were not comparable and showed a highly significant p-value of <0.0001.

The number of episodes of vomiting was comparable in all the four groups, with a p-value of 0.312, which is nonsignificant.

Summing up together the total episodes of nausea and vomiting in four groups, we categorized the episodes according to the hours postoperatively at which they occurred (Table 4 and Graph 3). Out of total 120 patients included in study, 78 patients experienced PONV. Maximum patients (46.15%) experienced nausea and vomiting within 0 to 4 hours postoperatively, 29 patients (37.17%) within 5 to 12 hours, and 13 patients (16.67%) beyond 12 hours till 24 hours. Also, the incidence was significantly higher in group M (38%) as compared with other groups. It was minimum in group P (6.4%), proving that patients of this group were most benefited in terms of PONV.

The test drug was given in the beginning of the surgery along with premedication before induction. The time at which first dose of rescue antiemetic given

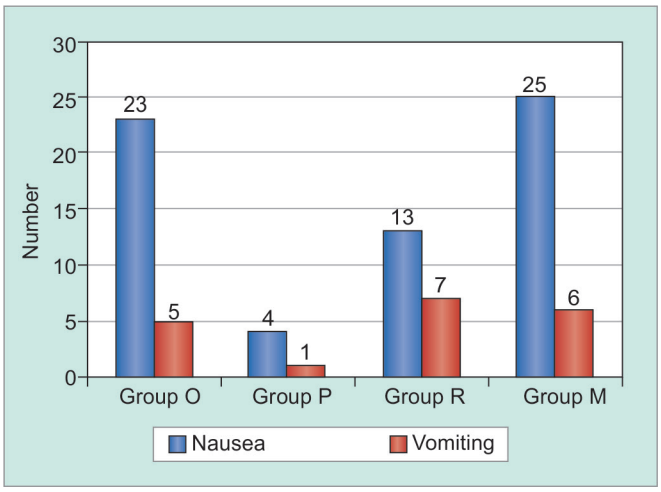
Table 3: Incidence of nausea and vomiting in each group

	Group O (%)	*Group P (%)*	*Group R (%)*	*Group M (%)*	*χ^2 value*	*p-value*
Nausea	18 (60.0)	4 (13.3)	13 (43.3)	24 (80.0)	25.44	<0.0001 (HS)
Vomiting	5 (16.7)	1 (3.3)	7 (23.3)	6 (20.0)	3.564	0.312 (NS)

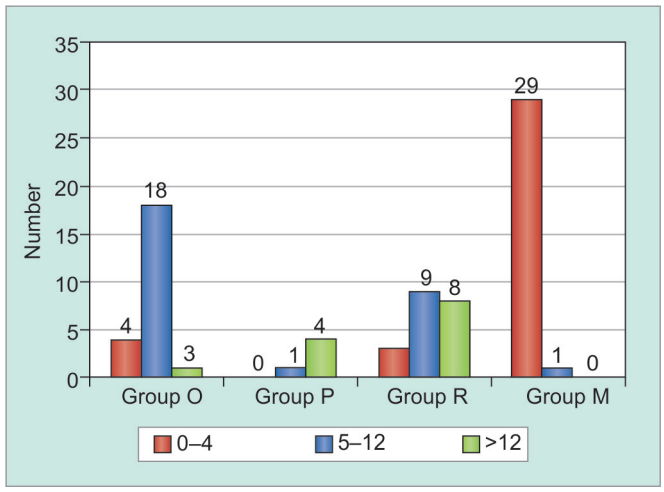
HS: Highly significant; NS: Nonsignificant

Table 4: Duration-wise incidence of nausea and vomiting

	Group O (%)	*Group P (%)*	*Group R (%)*	*Group M (%)*	*Total*	*χ^2 value*	*p-value*
0–4	4 (13.3)	0 (0)	3 (10.0)	29 (96.7)	36 (46.15)	79.84	0.000
5–12	18 (60.0)	1 (3.3)	9 (30.0)	1 (3.3)	29 (37.17)	31.42	0.000
>12	1 (3.3)	4 (13.3)	8 (26.7)	0 (0)	13 (16.67)	9.921	0.0192
Total	23 (29.48%)	5 (6.4%)	20 (25.6%)	30 (38.46%)	78		



Graph 2: Incidence of nausea and vomiting in each group



Graph 3: Duration wise incidence of nausea and vomiting in each group

Table 5: Duration after which first rescue antiemetic was given

	Group O	*Group P*	*Group R*	*Group M*	*F-value*	*p-value*
Duration (hours)	5.3 ± 4.43	21.6 ± 5.37	14.65 ± 8.62	1.22 ± 1.52	40.95	<0.0001 (HS)

HS: Highly significant

Table 6: Adverse effects in each group

Symptoms	*Group O (%)*	*Group P (%)*	*Group R (%)*	*Group M (%)*	*Total (%)*	*χ^2 value*	*p-value*
Headache	8 (26.7)	2 (6.7)	5 (16.7)	2 (6.7)	17 (14.17)	4.592	0.204 (NS)
Dizziness	5 (16.7)	3 (10.0)	3 (10.0)	6 (20.0)	17 (14.17)	0.754	0.860 (NS)
Allergic reaction	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	–	–
Total	13	5	8	8	34		

NS: Nonsignificant

on request of the patient was noted (Table 5). It gave an indirect measure of the duration of action of the drug. The mean duration at which it was given in group M is just 1.22 ± 1.52 hours, showing least efficacy of the drug of this group. The mean duration for group P was 21.6 ± 5.37 hours, showing its high efficacy in preventing PONV. All the four groups in this context showed a high significant variation with a p-value of <0.0001.

As evident from Table 6, the incidence of side effects was more in group O and least in group P.

DISCUSSION

In the present study, the antiemetic study drugs (ondansetron, palonosetron, ramosetron, and metoclopramide) were given to patients along with premedication. The hemodynamic parameters before induction, during surgery, and postoperatively were noted. It was concluded based on statistical analysis that there was no significant difference in the mean values of the measured hemodynamic parameters (heart rate, systolic blood pressure, diastolic blood pressure, and oxygen saturation) in preoperative, intraoperative, or postoperative period in all the four groups.

The present study showed that prophylactic antiemetic medication was well tolerated and provided clinically effective prevention of PONV, but the difference in their clinical efficacy and duration of action was found to be statistically significant. There were only few episodes of headache and dizziness, which were resolved as time relapsed without any specific treatment. No other hemodynamic, respiratory, or systemic effects of any drug were observed on any patient during the study period.

Palonosetron was statistically superior to other three drugs in the study for control of PONV. The overall incidence of nausea and vomiting was significantly higher in metoclopramide group. There were patients who experienced multiple episodes of nausea and vomiting. The study showed highly significant difference in first 0 to 4 hours ($p < 0.05$), which goes in accordance with shorter duration of action of metoclopramide. This was justified with the study conducted by Naguib et al.[11]

Out of 120 patients in the study, a total of 42 patients (35%) were completely relieved of PONV and did not require any rescue antiemetic for first 24 hours postoperatively. About 25 (83%) of total complete responders belonged to the group that received palonosetron and there were no complete responders in the group receiving metoclopramide. Ramosetron group had 10 (33.3%) complete responders, still less than patients in group P. This was in contrary to a study conducted by Swaika et al.[12]

The incidence of PONV was recorded in postoperative period for 24 hours. In this study, 30 (38.46%) patients out of 78 patients (partial responders and treatment failure) experienced nausea and vomiting who were given metoclopramide as antiemetic during premedication, and only 5 (6.7%) patients experienced PONV who received palonosetron. A total of 23 (29.48%) patients who received ondansetron experienced PONV. The efficacy of palonosetron has been proved in many studies like that conducted by Elahl and Badea in 2013, in which they concluded that administration of IV 0.075 mg of palonosetron to prevent PONV was very effective.[13]

The study showed significantly high efficacy of palonosetron as compared with ramosetron and ondansetron and least with metoclopramide (owing to its short duration of action, i.e., 1–2 hours) in prevention of PONV. High efficacy of palonosetron can be explained by strong binding to the serotonin receptors, making its effect last for a longer duration (72 hours). It is also evident from a comparative study of the efficacy of intravenous ondansetron and palonosetron for prevention of PONV conducted by Shadangi et al, who concluded that palonosetron is significantly more effective against PONV than ondansetron. It has a particularly more pronounced and prolonged effect on postoperative nausea.[14]

The adverse effects in all the groups were comparable. The incidence of headache was maximum in group O (26%), followed by group R (16.7%), and same for groups P and M (6.7%). Patients also complained of dizziness in postoperative period. About 20% of these were the ones who received metoclopramide as antiemetic and 16.7% were those who received ondansetron. Elahl and Badea[13] studied 62 patients undergoing middle ear surgery to compare effects of 0.075 mg for PONV as compared with placebo and showed adverse effects, such as headache, dizziness, and myalgia. There was no incidence of any allergic reaction or any other side effect during the study.

CONCLUSION

Many drugs have been used for preemptive antiemesis. Palonosetron is a second-generation 5-HT_3 antagonist with a longer duration of action. Ramosetron is a newer 5-HT_3 antagonist whose efficacy in prevention of PONV is still under study. We compared the above two drugs with ondansetron and metoclopramide, whose effect on PONV has already been well established.

The present study has shown the evidence of clinical effectiveness of palonosetron (0.075 mg) as an antiemetic for prophylaxis of PONV to be more as compared with ramosetron (0.3 mg), ondansetron (4 mg), and metoclopramide (10 mg) given IV for various surgical procedures under general anesthesia. Its effectiveness against PONV provides a new cost-effective agent to the present recital of antiemetic drugs.

The study also concludes that palonosetron may be a better option for prevention of postoperative nausea and vomiting in day care surgery as compared with ramosetron, ondansetron, and metoclopramide owing to its longer duration of action. Also, it serves an exemplar of an antiemetic with fewer side effects.

Hence, we conclude that palonosetron is a better option for PONV in patients for various surgeries under general anesthesia.

REFERENCES

1. Scuderi PE, Conlay LA. Postoperative nausea and vomiting and outcome. Int Anesthesiol Clin 2003 Fall;41(4):165-174.
2. Islam S, Jain PN. Postoperative nausea and vomiting (PONV): a review article. Indian J Anaesth 2004;48(4):253-258.
3. Furst SR, Rodarte A. Prophylactic antiemetic treatment with ondansetron in children undergoing tonsillectomy. Anesthesiology 1994 Oct;81(4):799-803.
4. Honkavaara P. Effect of Ondansetron on nausea and vomiting after middle ear surgery during general anesthesia. Br J Anaesth 1996 Feb;76(2):316-318.
5. Apfel CC, Kranke P, Eberhart LH, Roos A, Roewer N. Comparison of predictive models for postoperative nausea and vomiting. Br J Anaesth 2002 Feb;88(2):234-240.
6. Sinclair DR, Chung F, Mezei G. Can postoperative nausea and vomiting be predicted? Anesthesiology 1999 Jul;91(1):109-118.
7. Alon E, Himmelseher S. Ondansetron in the treatment of postoperative vomiting: a randomized, double-blind comparison with droperidol and metoclopramide. Anesth Analg 1992 Oct;75(4):561-565.
8. Jolley S. Managing post-operative nausea and vomiting. Nurs Stand 2001 Jun;15(40):47-52.
9. Rojas C, Stathis M, Thomas AG, Massuda EB, Alt J, Zhang J, Rubenstein E, Sebastiani S, Cantoreggi S, Snyder SH, et al. Palonosetron exhibits unique molecular interactions with the 5-HT3 receptor. Anesth Analg 2008 Aug;107(2):469-478.
10. Fukudo S, Ida M, Akiho H, Nakashima Y, Matsueda K. Effect of Ramosetron on stool consistency in male patients with irritable bowel syndrome with diarrhea. Clin Gastroenterol Hepatol 2014 Jun;12(6):953-959.
11. Naguib M, el Bakry AK, Khoshi MH, Channa AB, el Gammal M, el Gammal K, Elhattab YS, Attia M, Jaroudi R, Saddique A. Prophylactic antiemetic therapy with ondansetron, tropisetron, granisetron and metoclopramide in patients undergoing cholecystectomy. Can J Anaesth 1996 Mar;43(3):226-231.
12. Swaika S, Pal A, Chatterjee S, Saha D, Dawar N. Ondansetron, ramosetron, or palonosetron: which is a better choice of antiemetic to prevent postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Anesth Essays Res 2011 Jul-Dec;5(2):182-186.
13. Elahl MI, Badea M. Palonosetron in preventing postoperative nausea and vomiting in middle ear surgery (a randomized-controlled study). Egypt J Otolaryngol 2013;29(3):156-158.
14. Shadangi BK, Agrawal J, Pandey R, Kumar A, Jain S, Mittal R, Chorasia HK. A prospective, randomized, double-blind, comparative study of the efficacy of intravenous ondansetron and palonosetron for prevention of postoperative nausea and vomiting. Anaesth Pain Intensive Care 2013;17(1):55-58.