MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.59218/makrjp.2023.3.1.5

Comparative Study of Prophylactic Efficacy of Ondansetron and Palonosetron for Ponv in Patients Undergoing Modified Radical Mastectomy Under General Anaesthesia

[1]Bhairavi Nikhil Baljekar and [2]Anjali Pingle

[1]Department of Anaesthesia, Aster RV Hospital, J P Nagar Bengaluru, Karnataka 560078, India.

[2]Department of Anaesthesia, P D Hinduja National Hospital and Medical Research Centre, 8-12, Swatantryaveer Savarkar Rd, Mahim West, Mahim, Mumbai, Maharashtra 400016, India

OPEN ACCESS

Key Words
Ondansetron, palonosetron, breast surgery, rescue antiemetic

Corresponding Author
Bhairavi Nikhil Baljekar, Department of Anaesthesia, Aster RV Hospital, J P Nagar Bengaluru, Karnataka 560078, India

Author Designation
[1,2]Consultant

Received: 31 December 2023
Accepted: 15 January 2024
Published: 12 February 2024

Citation: Bhairavi Nikhil Baljekar, Anjali Pingle, 2024. Comparative study of prophylactic efficacy of Ondansetron and Palonosetron for PONV in patients undergoing modified radical mastectomy under general anaesthesia. Res. J. Pharm., 17: 1-5, doi: 10.59218/makrjp. 2023.3.1.5

ABSTRACT

The syndrome of nausea, retching and vomiting is collectively called Post Operative Nausea and Vomiting (PONV). PONV is also one of the most common causes of patient dissatisfaction after anaesthesia, with reported incidences of up to 30% in all post-surgical patients and up to 80% in high-risk patients. The present study was aimed at comparing prophylactic efficacy of Ondansetron and Palonosetron for PONV in patients undergoing modified radical mastectomy under general anaesthesia. Present study was prospective, randomized, double blinded study conducted in female patients, allocated to group O (received ondansetron 8 mg i.v. as prophylaxis prior to induction) and group P (received palonosetron 0.075 mg i.v. as prophylaxis prior to induction). The study population was equally divided into two groups each containing 93 patients. Age, Weight, Duration of surgery (min) and ASA grade (I/II) were comparable in both groups and difference was not significant statistically. Other characteristics such as history of receiving chemotherapy, h/o PONV and h/o motion sickness were comparable in both groups and difference was not significant statistically. ($p>0.05$) The two groups are comparable for the incidence of nausea, retching and vomiting in the 0-2, 2-6 and 6-24 hour postoperative period and difference was not significant statistically. ($p>0.05$). In our study, none of the patients had PONV in the 24– 72 hour period. The most frequent side effect was headache (3.76%), followed by headache with constipation (0.54%), constipation(0.54%) and giddiness (0.54%). Both the groups were comparable with respect to side effects, (p 0.534). The prophylactic efficacy of ondansetron and palonosetron as prophylaxis prior to induction, is comparable for PONV after breast surgery. The need for rescue antiemetic is comparable for the two drugs.

INTRODUCTION

Breast cancer is the most common malignant neoplasm seen all over the world[1]. Surgical resection with axillary lymph node dissection constitutes the primary treatment. Neoadjuvant and postoperative chemotherapy and/or radiation therapy form a part of the regime[1]. An incidence of 60-80% of PONV has been reported in patients undergoing mastectomy with axillary dissection with no prophylactic antiemetic[2,3]. Hence, prophylactic antiemetics are used in these surgeries. The syndrome of nausea, retching and vomiting is collectively called Postoperative Nausea and Vomiting (PONV). PONV has been characterized as the "big little problem[4]. PONV is also one of the most common causes of patient dissatisfaction after anaesthesia, with reported incidences of up to 30% in all post-surgical patients and up to 80 % in high-risk patients[5].

Most of the currently used antiemetics, including antihistamines, butyrophenones and dopamine receptor antagonists have been reported to cause occasional undesirable adverse effects, such as excessive sedation, hypotension, dry mouth, dysphoria, hallucinations and extrapyramidal signs[6]. Serotonin receptor antagonists are considered to be efficacious and with relatively fewer side effects[3]. Ondansetron, a serotonin receptor antagonist is commonly used in current clinical practice for PONV. Palonosetron, a third generation drug in this group has been reported to be superior in terms of efficacy and duration of action[7]. Present study was aimed to compare prophylactic efficacy of Ondansetron and Palonosetron for PONV in patients undergoing modified radical mastectomy under general anaesthesia

MATERIAL AND METHODS

Present study was a prospective, randomised, double blinded study conducted in the department of Anaesthesiology, at P. D Hinduja National Hospital and Medical Research Centre, Mumbai, India. Study duration was of 2 years (January 2011 to December 2013). Study approval was obtained from the institutional ethical committee.

Inclusion Criteria:

- Female patients, 18-75 years age, ASA grade I and II undergoing Modified Radical Mastectomy, willing to participate in present study

Exclusion Criteria:

- ASA grade III and IV patients
- Known hypersensitivity to ondansetron or palonosetron
- Prolonged QT interval on ECG
- Pregnant women
- Patients receiving any drug causing antiemesis in the last 24 hrs
- Patient refusal

Study was explained to patients in local language and written consent was taken for participation and study. The patient's history was recorded and pre-operative clinical assessment of each patient was done. Past history of PONV, motion sickness, history of chemotherapy, the number of cycles, the drugs used and the last date of chemotherapy. was noted. Investigations included complete blood count, fasting blood sugar, coagulation profile, urine routine, renal profile, serum electrolytes, liver profile, chest X-ray, ECG and any other specific investigations as indicated. The weight of the patient was recorded.

186 patients were randomly assigned by computer generated chits in group O (received ondansetron 8 mg i.v. as prophylaxis prior to induction) and group P (received palonosetron 0.075 mg i.v. as prophylaxis prior to induction). All patients underwent surgery under general anaesthesia with endotracheal intubation and controlled ventilation. Patients were monitored in the post anaesthesia care unit (PACU). Post operative pain was managed with intravenous paracetamol 15mg per kg, diclofenac sodium 1 mg per kg i.v. and if needed i.v. butorphanol 0.025 mg/kg as it has a relatively low incidence of nausea and vomiting compared to other opiods[8]. Patients were followed up for 72 hrs postoperatively at intervals of 0, 2, 6, 24 and72 hrs. The incidence of nausea, retching and vomiting for each patient over these time intervals was recorded. Patients were treated with metoclopramide 10 mg i.v. if they experienced vomiting. Complete response was defined as no nausea, retching or vomiting. Reversal was considered 0 hour and the intervals were calculated from this point.

After data collection, data entry was done in Excel. Data analysis was done with the help of SPSS Software version 15. Qualitative data has been presented with the help of frequency and percentage tables, association among study groups has been assessed with the help of Chi-Square and Fisher's exact test. $p<0.05$ is taken as significant.

RESULTS AND DISCUSSIONS

Study population was equally divided into two groups each containing 93 patients. Age, weight, duration of surgery (min) and ASA grade (I/II) were comparable in both groups and difference was not statistically significant ($p>0.05$). 14% of patients in group O received chemotherapy as compared to 17.2% in group P. 2.2 % in group O and 5.4 % in group P had history of PONV. Other characteristics such as history of receiving chemotherapy, h/o PONV and h/o motion

Table 1: General characteristics

Study Parameter	Group O	Group P	p-value
Age	56.83 ± 11.39	55.06±12.71	0.320
Weight	68.37±13.41	65.17±12.21	0.091
Duration(min)	148.98±32.84	151.88±31.66	0.540
ASA grade			
I	33 (35.5 %)	48 (52.5 %)	0.765
II	60 (64.5 %)	45 (47.3 %)	
Past history			
History of receiving **chemotherapy**	13 (14 %)	16 (17.2 %)	0.544
h/o PONV	2 (2.2 %)	5 (5.4 %)	0.248
h/o motion sickness	1 (1.1 %)	4 (4.3 %)	0.366

Table 2: Incidence of PONV

Study group	Nausea no. of percentage	Retching no. of percentage	Vomiting no. of percentage	Complete Response (no.)	p-value
Postoperative Time period 0-2 hrs					
Group O	10 (9.7)	4 (4.3)	3 (3.2)	87.9	0.733
Group P	8 (8.6)	5 (5.4)	4 (4.3)	87.9	
Postoperative Time period 2-6 hrs			-		
Group O	5 (5.4)	2 (2.2)	1 (1.1)	93.5	0.248
Group P	7 (7.5)	5 (5.4)	5 (5.4)	88.1	
Postoperative Time period 6-24 hrs					
Group O	2 (2.2)	1 (1.1)	0 (0)	98.4	0.316
Group P	1 (1.1)	0 (0)	0 (0)	99.5	

Table 3: Need for rescue antiemetic and Complete response

Study Parameter	Group O	Group P	p-value
Need for rescue antiemetic	4 (4.3)	7 (7.5)	0.682
Complete response	80 (86)	78 (83.9)	0.351

Table 4: Risk factors and incidence of PONV

Additional Risk Factor	No. of Patients	Incidence of PONV (no.)	Incidence in percentage	Fishers exact t test, p value
None	148	17	11.48	Reference group
h/o chemotherapy	25	2	8	0.4591
h/o motion sickness	4	0	0	0.6190
h/o PONV	5	5	100	0.00004
h/o chemotherapy and motion sickness	2	2	100	0.0153
h/o chemotherapy and PONV	2	2	100	0.0153

Table 5: Side effects

	side effects				
Study group	No.	Headache	Headache and constipation	Constipation	Giddiness
Group O	88 (94.6)	4 (4.3)	0 (0.0)	1 (1.1)	0 (0.0)
Group P	88 (94.6)	3 (3.2)	1 (1.1)	0 (0.0)	1 (1.1)
Total	176 (94.62)	7 (3.76)	1 (0.54)	1 (0.54)	1 (0.54)
Chi-Square Tests	Value	df	p-value		
Pearson Chi-Square	3.143	4	0.534		

sickness were comparable in both groups and difference was not significant statistically (p>0.05). The two groups are comparable for the incidence of nausea, retching and vomiting in the 0-2, 2-6 and 6-24 hour postoperative period and difference was not significant statistically (p>0.05).In our study, none of the patients had PONV in the 24-72 hour period. In the present study, need for rescue antiemetic and complete response were comparable in both groups and difference was not significant statistically (p>0.05).

There was an increased incidence of PONV in the subset of patients with additional risk factors like past history of PONV and more than two risk factors as shown above. There was no significant correlation between incidence of PONV and previous h/o chemotherapy and motion sickness. Most frequent side effect was headache (3.76%), followed by headache with constipation (0.54%), constipation(0.54%) and giddiness (0.54%). Both the groups were comparable with respect to side effects, (p 0.534).PONV has physical, surgical and anaesthetic consequences as described below. It also has financial implications for the hospitals or institutions. Physical consequences include sweating, pallor, tachycardia, esophageal tear, wound dehiscence and electrolyte imbalance[6]. Surgical consequences include disruption of vascular anastomoses and increased intracranial pressure. The anaesthetic consequences are aspiration pneumonitis and discomfort in recovery. For institutions, there is an increased financial burden because of increased nursing care, delayed discharge from recovery units and unexpected admissions for overnight stay.

PONV is one of the most distressing symptoms after general anaesthesia. It has been estimated that the incidence of PONV worldwide is 30 % and increases to 70 to 80 % in high risk patients[9]. In a survey conducted by Macario[10]. vomiting has been rated as the most undesirable symptom postoperatively.[11] It has been estimated that 0.2% of patients experience

intractable PONV and each episode of vomiting delays discharge from post anaesthesia care unit by 25 mins[11].

A variety of drugs have been developed to tackle PONV. The consensus guidelines by the Society of Ambulatory Anaesthesia 2007, recommend 5HT-3 receptor antagonists as the first line of prophylaxis for PONV under general anaesthesia[12]. They are highly efficacious and have minimal side effects. The Society of Ambulatory Anaesthesia Guidelines for management of PONV 2007 suggest that 5HT-3 receptor antagonists are most effective when given at the end of the surgery[12]. In this study, the incidence of PONV over a period of 72 hours was 14% with ondansetron as compared to 16.1% with palonosetron which was statistically insignificant (p = 0.682). Thus, the antiemetic efficacy of both the drugs is comparable in patients undergoing MRM.

In our study, none of the patients experienced PONV after 24 hours. Baja S.S.*et al*[13]. found that palonosetron to be a better antiemetic with reduced requirement of rescue antiemetic. Park S.K.*et al*[14]. found palonosetron to be a better antiemetic as it had statistically better complete response and incidence of nausea, but need for rescue antiemetic, severity of nausea and adverse effects were comparable between the two. Laha B. *et al*[15]. found no significant difference between ondansetron and palonosetron, in terms of efficacy, need for rescue antiemetic and adverse effects. In a trial by Moon Y.E. *et al*.[16] noted that, palonosetron was found to have superior efficacy and reduced requirement of rescue antiemetic as compared to ondansetron. Thus, even with its higher binding affinity and longer half-life, the efficacy of palonosetron as compared to ondansetron for PONV has been shown to be variable[17]. This is unlike studies conducted for nausea and vomiting post chemotherapy, where palonosetron seems to be superior to other 5HT-3 antagonists. Chemotherapy leads to release of serotonin mainly from the gut whereas PONV is multifactorial and the exact mechanism is still not clear[17].

When we analysed the incidence of PONV across both groups, we found that the incidence of overall nausea was 17.7%, 9.1% for retching and 7.5% for vomiting. The complete response rates with palonosetron and ondansetron was 83.9% and 86% respectively in our study. A similar incidence was found by Baja *et al*. noted that incidence of nausea and vomiting were 20% and 13.3% for the ondansetron group respectively; whereas it was 6.7% and 3.3% respectively for the palonosetron group. We observed that when the incidence of PONV was analysed for the 0-72 hour period, the highest incidence was found in the 0-2 hour immediate postoperative period. This could be explained by the residual effect of inhalational anaesthetics.

The need for rescue antiemetic was 4.3% with ondansetron and 7.5 % with palonosetron which was statistically insignificant (p = 0.870). In a study conducted by Baja *et al*.13 there was significant difference in the dose required for rescue antiemesis. The group which received ondansetron needed 10.6 mg as compared to 6.4 mg in the palonosetron group which was clinically significant. The most common side effects in both groups were headache (3.8%) followed by constipation (0.5 %) and giddiness (0.5%). The incidence of side-effects was comparable in the two groups, 4.3% for ondansetron and 3.2% for palonosetron. Thus, both drugs appear to be safe.

There were a few limitations of this study. The equipotent dose of ondansetron and palonosetron has not yet been determined. The optimal doses of ondansetron and palonosetron which have been used are based on previous studies. As a placebo was not used, the incidence of PONV in patients undergoing MRM could not be calculated. Though postoperative pain scores were not recorded, the analgesic requirement in both groups was similar. Both drugs act on different receptor subtypes and ondansetron has additional binding capacity for other receptors. The clinical relevance of this is unknown. The antiemetic efficacy of drugs can vary with the site and type of surgical intervention.

CONCLUSION

The prophylactic efficacy of ondansetron and palonosetron as prophylaxis prior to induction, is comparable for PONV after breast surgery. The need for rescue antiemetic is comparable for the two drugs. The side effect profile of the two drugs is comparable and both drugs appear to be safe.

REFERENCE

1. Gómez-Hernández, J., A.L. Orozco-Alatorre, M. Domínguez-Contreras, A. Oceguera-Villa nueva and S. Gómez-Romo *et al*. 2010. Preoperative dexamethasone reduces postoperative pain, nausea and vomiting following mastectomy for breast cancer. BMC. Cancer., Vol. 10. 10.1186/1471-2407-10-692
2. Sadhasivam, S., A. Saxena, S. Kathirvel, T.R. Kannan, A. Trikha and V. Mohan, 1999. The safety and efficacy of prophylactic ondansetron in patients undergoing modified radical mastectomy. Anesth. Analg., 89: 1340-1345.
3. Hammas, B., S. Thörn and M. Wattwil, 2002. Superior prolonged antiemetic prophylaxis with a four-drug multimodal regimen-comparison with propofol or placebo. Acta. Anaesth. Scand., 46: 232-237.
4. Kapur, P.A., 1991. The big' little problem. Anesth. Analg., 73: 243-245.

5. Pierre, S. and R. Whelan, 2013. Nausea and vomiting after surgery. Contin. Educ. Anaesth. Crit. Care. Pain., 13: 28-32.
6. Watcha, M.F. and P.F. White, 1992. Postoperative nausea and vomiting. Anesthesiol., 77: 162-184.
7. Muchatuta, N.,A.M.J. and Paech, 2009. Management of postoperative nausea vomiting: Focus on palonosetron. Ther. Clin. Risk. Manag., 5: 521-534.
8. WHO., 2006. Critical review of Butorphanol., https://ecddrepository.org/sites/default/files/2023-04/4.1buthorphanolcritreview.pdf.
9. Smith. H.,S. E.J. and Smith, 2012. Postoperative nausea and vomiting. Ann. Palliat. Med., 1: 94-102
10. Macario, A., M. Weinger, S. Carney and A. Kim, 1999. Which clinical anesthesia outcomes are important to avoid. the perspective of patients. Anesth. Analg., 89: 652-658.
11. Chatterjee, S., A. Rudra and S. Sengupta, 2011. Current concepts in the management of postoperative nausea and vomiting. Anesthesiol. Res. Pract., 2011: 1-10.
12. Gan, T.J., T.A. Meyer, C.C. Apfel, F. Chung and P.J. Davis *et al*. 2007. Society for ambulatory anesthesia guidelines for the management of postoperative nausea and vomiting. Anesth. Analg., 105: 1615-1628.
13. Bajwa, S., S. Bajwa, J. Kaur, V. Sharma and A. Singh *et al*. 2011. Palonosetron: A novel approach to control postoperative nausea and vomiting in day care surgery. Saudi. J. Anaesth., 5: 19-24.
14. Park, S.K., E.J. Cho, S.H. Kang, Y.J. Lee and D.A. Kim, 2013. 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., 64: 133-137.
15. Laha, B., A. Hazra and S. Mallick, 2013. Evaluation of antiemetic effect of intravenous palonosetron versus intravenous ondansetron in laparoscopic cholecystectomy: A randomized controlled trial. Indian. J. Pharmacol., 45: 24-29.
16. Moon, Y.E., J. Joo, J.E. Kim and Y. Lee, 2012. Anti-emetic effect of ondansetron and palonosetron in thyroidectomy: A prospective, randomized, double-blind study. Br. J. Anaesth., 108: 417-422.
17. Pal, A., S. Swaika, S. Chatterjee, D. Saha and N. Dawar, 2011. 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., 5: 182-186