Section: Anesthesiology

Original Research Article

COMPARATIVE EVALUATION OF INTRAVENOUS ONDANSETRON(4MG) VERSUS INTRAVENOUS PALANOSETRON(75MCG) IN THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN LAPARASCOPIC GYNAECOLOGICAL SURGERIES

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Received *: 10/11/2023*
Received in revised form *: 06/01/2024*
Accepted *: 23/01/2024*

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DOI:10.5530/ijmedph.2024.1.58

Source of Support: Nil,
Conflict of Interest: Nonedeclared

Int J Med Pub Health
2024; 14 (1); 305-310

ABSTRACT

Background: This single blinded interventional prospective study compares intravenous Ondansetron and Palonosetron in preventing postoperative nausea and vomiting in patients undergoing laparoscopic gynaecological surgeries under general anesthesia.

Material and Methods: This study was conducted at Government Kasturba Gandhi Hospital for Women and Children, Madras Medical College, Chennai. Instituitional Ethical committee approval was obtained before preceding the study. Informed Written consent was obtained from all the100 patients who were scheduled to undergo elective laparoscopic gynaecological surgery. Information about the study type, the drug, its benefits and side effects were clearly explained and willingness of the patient to participate in the study was documented.

Results: Study population of 100 patients undergoing elective laparoscopic gynecological surgeries were randomly divided into two groups. 50 patients were allotted to group O receiving Ondansetron and 50 patients were allotted to group P receiving Palonosetron. Statistical analysis was done using SPSS package version 17 for windows. To compare intergroup differences, student's T test was used and for Categorical variables chi square or fisher's exact test was used. A P value less than 0.05 was considered to be statistically significant.

Conclusion: It is concluded that Intravenous Palonosetron is more effective than intravenous Ondansetron in the prevention of post-operative nausea and vomiting. The number and frequency of emetic episodes were significantly reduced. Hence Palonosetron is superior to Ondansetron and it is safe and reliable to use in the prevention of post-operative nausea and vomiting.

Keywords: Surgery, nausea, post-Operative vomiting, anaesthetic.

INTRODUCTION

Post-Operative Nausea and Vomiting is defined as nausea, retching or vomiting that occurs during first 24-48hrs after surgery. Post-Operative Nausea and Vomiting is the second most common complaint next to pain in the post- operative period. In the Era of Advanced Medicine and improved Post-Operative care, Nausea and Vomiting in post-operative period is a distressing complication which needs attention and prevention. Of various pathways and triggering factors that have been postulated so far, no exact etiology has been defined.[1-3]

Numerous factors have been identified to be associated with Post-Operative Nausea and vomiting such as patient, age, gender, type of surgery, duration of surgery, anesthetic factors, smoking, History of motion Sickness, etc.[4]

Among the anaesthesia risk factors inhaled anaesthetics and opioids are the common triggering agents associated with post-operative nausea and vomiting. Post-operative nausea and vomiting being an unpleasant experience subjectively, is also associated with rare but serious adverse medical complication such as aspiration, wound and suture dehiscence in case of major abdominal surgeries, esophageal rupture, subcutaneous emphysema, and pneumothorax. Post-operative nausea and vomiting is also reported to be the common cause of hospital admission following day care surgeries.[5-7]

Hence the hunt for an effective antiemetic, thirst for a greater understanding and insight in the prevention and treatment of postoperative nausea and vomiting is reflected in the numerous studies that has been conducted so far. Currently available antiemetic drugs include Dopamine antagonist such as Metoclopramide, Droperidol, haloperidol, H1 receptor antagonist.[8,9]

The aim of this single blinded interventional prospective study is to compare the effectiveness of intravenous ondansetron (4mg) vs intravenous palonosetron (0.075mg)in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic gynecological surgery under general anaesthesia.

MATERIAL AND METHODS

This was a randomized single blinded interventional study conducted at Government Kasturba Gandhi Hospital for Women and Children, Madras Medical College, Chennai. Institutional Ethical committee approval was obtained before preceding the study. Informed Written consent was obtained from all the100 patients who were scheduled to undergo elective laparoscopic gynecological surgery. Information about the study type, the drug, its benefits and side effects were clearly explained and willingness of the patient to participate in the study was documented.

The inclusion criteria for the patients in the study group were age more than 18 years and above, ASA PS1&2, patients undergoing elective Surgeries with mallampatiscore1&2 and patients who are willing to undergo the study and those who have given written informed consent.

The exclusion criteria include patients posted for emergency surgery, Lack of written informed consent, Pregnant female, History of seizures and any Neurological deficit, History of motion sickness, History of nausea and vomiting 24hrs prior to surgery. Patients with history of significant cardiovascular disease or rhythm disturbance, liver, renal and endocrine abnormalities were excluded from the study.

Study population of 100 patients were randomly assigned into two groups of 50 each.Group O received 4mg of Ondansetron and Group P received 0.075 mg of Palonosetron intravenously before the induction of Anesthesia. The drug was administered by the Anesthesiologist who was involved in the assessment of the patient. In all the patients undergoing study, standardized anesthesia technique was followed.

All patients received premedication with Injection glycopyrrolate0.004mg/kgand Injection fentanyl 20 mcg/kg. Intravenously 30 mins prior to induction. The study drug was administered according to the group. Anesthesia was induced with Injection thiopentone at a dose of 5-6 mg/kg. Intubation was facilitated with Injection atracurium 0.5 mg/kg.PVC endotracheal tube was used for induction. Anaesthesia was maintained with Oxygen and Nitrous oxide mixture in a ratio of 1:3 and the volatile anaesthetic used for maintenance was sevoflurane, the concentration of which was titrated between 1-2% according to the depth of Anesthesia.

Intraoperatively muscle relaxation was maintained with Injection Atracurium 0.08mg/kg. Hemodynamic stability in the intra operative period was monitored with heart rate, blood pressure, spo2 monitor. ETCo2 monitoring was also done.

Intraoperatively, the gas used for in sufflation during laparoscopy was carbondioxide. Intra-abdominal pressure was maintained between 14-16mmHg.Heart rate and blood pressure was maintained within 20% of the preoperative values. Neuromuscular blockade was reversed with Injection Neostigmine 0.04mg/kg and Injection Glycopyrrolate 0.005mg/kg.In the immediate post-operative period patient was shifted to recovery room for monitoring of vitals which includes heart rate, ECG, SpO2.

Patients were followed up for the incidence of nausea and vomiting immediately after extubation, during first 24 hrs and then over a period of 24-48 hours. patients were asked whether they had nausea and vomiting and other complaints like headache,

Dizziness and constipation. The complaints in the follow up period was recorded by the staff nurse. Data obtained were analyzed and the statistical results were obtained using SPSS software.

RESULTS

Study population of 100 patients undergoing elective laparoscopic gynecological surgeries were randomly divided into two groups. 50 patients were allotted to group O receiving Ondansetron and 50 patients were allotted to group P receiving Palonosetron.

Statistical analysis was done using SPSS package version 17 for windows. To compare intergroup differences, student's T test was used and for Categorical variables chi square or fisher's exact test was used. A P value less than 0.05 was considered to be statistically significant.

Age distribution

Female patients aged18 years and above were included in this study.

Patients under 40 years of age comprised the majority of study population.The Pvalue is 0.596 and there is no statistically significant difference in the age of the patients between the two study groups. [Table 1]

The average distribution of weight in Ondansetron group is 55.16 and Palonosetron group is 57.16. The P value based on student's T test is 0.162 which is not statistically different. The two groups were comparable in weight distribution. [Table 2]

Patients belonging to the ASA physicalstatus1&2 were included in the study group.

Based on T test the p value is 1.000.Hence there is no statistical difference between the two groups and they are comparable. [Table 3]

Based on T test, P value is 0.089.there is no statistical difference between the two groups and hence they are comparable in terms of duration of surgery. [Table 4]

Based on T test for equality of means the P value was found to be 0.182. There was no statistical significance between the two groups and the duration of anaesthesia was comparable between two groups. [Table 5]

Nausea (0-2hour)

The incidence of nausea was 8 % in the Ondansetron group when compared to 4% in the Palonosetron group. With respect to the incidence of nausea in the first two hours of the post-operative period, patients in O (Ondansetron) group had no significant difference in the incidence of nausea when compared to patients in the P(Palonosetron) group with a P value of 0.395 by chi – square test. Comparison of incidence of nausea (0-2hr) (chi – square test).

Three patients in group O reported nausea and there was no incidence of nausea in the Palonosetron group in 2-24 hrs. [Table 6]

The P value by chi-square test was0.039.The difference in the incidence of nausea over period of 2- 24 hrs was statistically significant with the incidence of 6%. Nausea in the Ondansetron group compared to Palonosetron group with no incidence of nausea. [Table 7]

NAUSEA (24-48HOURS)

With the incidence of 4% (2 patients) nausea in Ondansetron group compared to nil incidence of nausea in Palonosetron group over a period of 24-48 hours, the P value was found to be 0.093 by chi-square test which implies that there is no statistically significant difference between the two groups.

Vomiting (0-2hours)

The incidence of vomiting in ondansetron group is 18% (9 Patients) and 8% (4 Patients)in palonosetron group. By statistical analysis using chi-square test the p value was found to be 0.137 and hence there is no statistical difference in the incidence of vomiting in the immediate two hours following surgery. [Table 8]

Vomiting (2to24Hours)

With respect to the incidence of vomiting in 2 to 24 hours, it was found that group O had12% incidence (6 Patients) whereas group P had 2% incidence (1 Patient). The difference in the incidence of vomiting between the two groups was significant with the P value of 0.050 (Chi – Square test). [Table 9]

VOMITING (24–48Hours)

In the analysis of incidence of vomiting over a period of 22 to 48 hours, it was found that the incidence is 6% in Ondansetron group compared to nil incidence of vomiting in Palonosetron group. The P value by fisher's exact test was found to be 0.039 and statistically significant difference between the two groups was observed. [Table 10]

Comparison of vomiting (24–48 Hours)

Complete response to nausea

Complete response to nausea was found to be 84% in Ondansetron group when compared to 96% in Palanosetron group. With the P value of 0.046%, significant difference in complete response to nausea was found between the two groups. [Table 11]

Complete response to vomiting

In comparing the complete response to vomiting, it was found that complete response was 66% (17 Patients) in Ondansetron group and it was 90% (5 Patients)in Palanosetron group. The P value by chi-square test was found to be 0.04 and it was a highly significant statistical difference between the two groups. [Table 12]

Comparison of Complete response to vomiting (Chi – square test)

Headache:

The incidence if headache was 8% (4Patients) in Ondansetron group and 6% (3 Patients) in Palonosetron group. The two groups were comparable with P value of 0.695. [Table 13]

Dizziness

The incidence of dizziness was 6% (3Patients) in both groups and there is no difference between the two groups with the P value of 1.000. [Table 14]

Constipation

We found that 4% of study subjects in Ondansetron group had constipation where as it was 2% in Palonosetron group without any statistical difference (p value 0.558). [Table 15]

Table 1: Age distribution

AGE(YEARS)				
Group	N	Mean	Std.Deviation	P VALUE
O	50	37.08	11.803	
P	50	35.94	9.513	0.596

Table 2: Weight Distribution

Group	Mean	Standard Deviation	P Value
O	55.16	9.63	0.162
P	57.76	8.79	

Table 3: ASA physical status

GROUP	PS1	PS2	P Value
O	37	13	1.000
P	37	13	

Table 4: Duration of Surgery:

Duration of surgery			
Group	Mean	Standard Deviation	P Value
O	69.86	32.07	0.089
P	59.36	28.92	

Table 5: Duration of Anesthesia

DURATIONOFANAESTHESIA			
Group	Mean (Min)	Standard Deviation	P Value
O	86.92	32.91	0.182
P	78.16	32.33	

Table 6: Nausea

NAUSEA(0-2HOUR)				
GROUP	0	P	TOTAL	P VALUE
+	4	2	6	
	(8%)	(4%)	(6%)	
-	46	48	94	0.395
	(48.9%)	(51.1%)	(94%)	

Table 7: NAUSEA (2-24HOURS)

GROUP	O	P	P VALUE
+	3(6%)	0(0%)	
_	47(94%)	50(100%)	0.039

Table 8: Comparison of Nausea(24-48hours)

GROUP	O	P	P VALUE
+	2(4%)	0(0%)	
-	48(96%)	50(100%)	0.093

Table 9: Comparison of vomiting 0 to 2 Hrs

Group	O	P	P VALUE
+	9(18%)	4(8%)	0.137
-	41(82%)	46(92%)	

Table 10. Vomiting (2to24Hours)

GROUP	O	P	P VALUE
+	6(12%)	1(2%)	0.050
-	44(88%)	49(98%)	

Table 11: Vomiting (2 to 24 Hours)

GROUP	O	P	P VALUE
+	6(12%)	1(2%)	0.050
-	44(88%)	49(98%)	

Table 12: Complete response to nausea

GROUP	O	P	P VALUE
+	8(16%)	2(4%)	0.046
-	42(84%)	48(96%)	

Table 13: Complete response to vomiting

GROUP	O	P	P VALUE
+	17(34%)	5(10%)	0.004
-	33(66%)	45(90%)	

Table 14: Headache

GROUP	O	P	P VALUE
+	4(8%)	3(6%)	0.695
-	46(92%)	47(94%)	

Table 15: Dizziness

GROUP	O	P	P VALUE
+	3(6%)	3(6%)	1.000
-	47(94%)	47(94%)	

Table 16: Constipation

GROUP	O	P	P VALUE
+	2	1	
	(4%)	(2%)	
			0.558
-	48	49	
	(96%)	(98%)	

DISCUSSION

Nausea and vomiting in the post-operative period is a distressing complication following General Anesthesia. Incidence of Nausea and vomiting in the post-operative period delays the discharge of the patient undergoing day care surgeries. Hence, the search for an effective antiemetic is reflected in the numerous studies that have been carried out so far.[10]Since the mechanism and the pathway involved in nausea and vomiting is complex, no single drug can serve the purpose of completely preventing nausea and vomiting. The definite risk factors for the incidence of post-operative nausea and vomiting include age, gender, duration and the type of anesthesia, obesity, nonsmokers, meniere's disease, history of motion sickness and history of post-operative nausea and vomiting. The increased usage of volatile anesthetics in General anaesthesia and opioids for postoperative analgesia has increased the incidence of post-operative nausea and vomiting.[11,12]

Currently 5HT3 receptor antagonists are used as first line antiemetics in the prevention of post-operative nausea and vomiting. Among serotonin receptor antagonist, Ondansetron is the first drug of choice. Second generation drug Palonosetron is unique among the serotonin receptor antagonist because of its allosteric binding at the receptor site with receptor internalization and a prolonged duration of action of around 40 hours.[13,14]

In the present study, the efficacy of Palonosetron is compared with Ondansetron in the prevention of post-operative nausea and vomiting in patients undergoing Laparoscopic gynaecological surgery. The risk factor in the subjects include female patients, laparoscopy and gynecological procedures which is significantly associated with the incidence of nausea and vomiting. In the current era of minimally invasive surgeries aiming at discharge on the day of surgery, an effective anti-emetic with greater potency and longer half-life is required. As discussed above, Palonosetron meets the above criteria and it is superior among the serotonin (5HT3) receptor antagonist in terms of potency and half-life.[15,16]

In this study, we compared the potency, antiemetic effect and adverse effect profile of intravenous Ondansetron and Palonosetron. We found that Palonosetron is superior to ondansetron in the prevention of nausea and vomiting. The incidence of vomiting is 34% in the Ondansetron group when compared to 10% in the Palonosetron group. The incidence of nausea is16% in Ondansetron group when compared to 4% in the Palonosetron group.[17,18]

We found that there was no difference in the incidence of nausea and vomiting between the groups in the first 0-2 hours and it is significantly reduced in palonosetron group when compared to ondansetron group in the 2-48 hours. Vomiting occurred in13.3%patients in ondansetron group ant it was 3.3% in palonosetron group which is less when compared to our study. The incidence of vomiting in ondansetron and palonosetron group is 20% and 6% in their study when compared to 16% and 4%respectively in our study. Reduction in nausea and emetic episodes in their study could be due to the use of Propofol for induction and maintenance of anesthesia which possess antiemetic effect even at very low doses. The results of their study correlate with our study which shows that Palonosetron is superior to Ondansetron in the prevention of nausea and vomiting.[19-21]

Moon Y et al reported that the incidence of PONV is 62% in Ondansetron group compared to 42% in palonosetron group in the study of patients who received opioid based patient controlled analgesia. The incidence of PONV is comparatively higher than in our study. This could be probably due to the continuous use of opioids in the postoperative period. The results obtained from the study are similar to our results which prove that Palonosetron is superior to Ondansetron in the prevention of post-operative nausea and vomiting.[22-24]

We found that the incidence of adverse effect such as headache, constipation and dizziness is similar in both groups. This correlates with the reports of other

studies in relation to the adverse effect profile of the two drugs under study.[25,26]

There was no incidence of life threatening rhythm abnormalities like prolonged QT interval in our study. Food and drug administration has recently issued black box alert for ondansetron in view of prolongation of QT interval. However, no such incidence has been reported in palonosetron so far. Based on observation and analysis, Palonosetron was found to be superior to ondansetron in the prevention of Nausea and vomiting. Hence, single intravenous dose of 0.075mg Palonosetron before the induction of anaesthesia is the preferred drug in the prevention of nausea and vomiting.[25-27]

CONCLUSION

It is concluded that Intravenous Palonosetron (75 mcg) is more effective than intravenous Ondansetron(4mg) in the prevention of postoperative nausea and vomiting. The number and frequency of emetic episodes were significantly reduced. Hence Palonosetron is superior to Ondansetron and it is safe and reliable to use in the prevention of post-operative nausea and vomiting.

Funding: None

Conflict of Interest: None.

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