Comparison of Effect of Ondansetron VS Palonosetron in Prevention of Postoperative Nausea and Vomiting Following Laparoscopic Surgery

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ABSTRACT

Introduction: Palonosetron is a new second-generation selective 5-hydroxytryptamine type 3 receptor antagonists that reportedly has more potent antiemetic effect. Present study was undertaken to compare the efficacy of Palonosetron in the prevention of postoperative nausea and vomiting (PONV) with that of Ondansetron in patients undergoing laparoscopic surgery.

Material and Methods: In this prospective study, 50 healthy patients who were undergoing laparoscopic operation were divided into two groups: ThePalonosetron group (0.075 mg i.v.; n=25) and the Ondansetron group (8 mg i.v.; n=25). The treatments were given 30 minutes before the end of surgery. The incidence of PONV, severity of nausea, and the use of rescue antiemetic requirements during the first 24 h after surgery were evaluated as two groups (0-6 hours and 6-24 hours).

Results: The incidence of nausea in the first 6 hours after the surgery in the Palonosetron and Ondansetron groups was 4% and 20% respectively, which was statistically insignificant whereas late nausea (6-24 hrs.) was 12% and 40% which was statistically significant. 2 patients in the Ondansetron group and none in the Palonosetron group had vomiting during the first 6 hours, which was statistically insignificant, whereas none in the Palonosetron group and 32% of patients in Ondansetron group had vomiting during the late postoperative period of 6-24 hours which was statistically significant.

Conclusions: Palonosetron0.075 mg i.v.was found to be more effective than Ondansetron 8 mg i.v.in prevention of PONV in the 6-24 hours' period after theLaparoscopic surgery.

Key Words: Post-operative, Nausea and Vomiting, Palonosetron, Ondansetron, Laparoscopic surgery

INTRODUCTION

Postoperative nausea and vomiting is one of the most common and distressing side effect encountered by patients following anesthetic and surgical procedures. In the present scenario, it is estimated that 20 to 30% of adult patients develop postoperative emesis[1], which is consistently lower when compared to 75 to 80% reported during the ether era. Incidence of postoperative nausea and vomiting ranges from 25 to 55% following inpatient surgery and 8 to 47% for outpatient surgery. When questioned before surgery, it was observed that patients were concerned about postoperative nausea and vomiting apart from pain and often rate it worse than postoperative pain.[2] Severe and persistent postoperative nausea and vomiting can cause tension on suture lines, bleeding at operative sites and wound dehiscence, venous hypertension, esophageal tears and rupture, rib fractures, gastric herniation and muscular fatigue.[3]

In neurosurgical cases, postoperative nausea and vomiting can cause increased intracranial tension. It can also increase the risk of pulmonary aspiration. It may result in dehydration and electrolyte imbalance in pediatric population.Postoperative nausea and vomiting is a major contributor to burgeoning health care costs for both the hospital and the patient. These costs may result from longer recovery, extended stay in the hospital, added attention required from nurses and physicians, additional drug supplies as well as unanticipated admissions following outpatient procedures.[4,5] Most of the currently used antiemetic drugs like antihistaminic, anticholinergics and dopamine receptor antagonists possess clinically significant side effects.[6]

Palonosetron[7-10] is a new second generation selective 5-hydroxytryptamine type 3 ($5HT_3$) receptor antagonist that reportedly has more potent antiemetic effects compared with other $5HT_3$ receptor antagonists. The purpose of this study was to evaluate the efficacy of Palonosetron for the prevention of postoperative nausea and vomiting (PONV) with that of Ondansetron in patients undergoing laparoscopic surgery. The aim of the present study is to compare the effectiveness of intravenously administered Palonosetron and Ondansetron in the prevention of postoperative nausea and vomiting in patients following laparoscopic surgery under general anesthesia.

MATERIAL AND METHODS

The study was approved by the hospital ethics committee and written informed consent was obtained from patients. A total number of 50 patients in the age group of 26 to 55 years belonging to ASA Grade I and ASA Grade II undergoing laparoscopic surgery under general anesthesia were selected for the present study. They were randomly divided into two groups, Group A and Group B, each consisting of 25 pa-

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tients. Group A received 0.075 mg of Palonosetroni.v.and group B received 8 mg of Ondansetroni.v., 30 minutes before the reversal of anesthesia.

Selection of patients

A] Inclusion criteria

1: Patients of ASA Grades I, and II.
2: Patients between the age group of 26 to 55 years.

B] Exclusion criteria

1: Patients belong to ASA Grade III, IV and V.
2: Patients below the age of 26 years.
3: Patients above the age of 55 years.
4: Patients with a history of hypersensitivity to Ondansetron or
Palonosetron and those with a history of motion sickness.
5: Patients with recent or chronic ingestion of any other medicine with potential antiemetic properties.
6: Patients with clinically significant cardiovascular, pulmonary, renal, hepatic, neurological or endocrine abnormalities.

Preoperative visit was conducted on the previous day of surgery and a detailed history and present complaints were noted. General and systemic examinations of cardiovascular, respiratory and central nervous system were done. Routine laboratory investigations like complete haemogram, blood urea, serum creatinine, and blood sugar, ECG, bleeding time and clotting time were done. Preoperative data collected included age, weight, heart rate, blood pressure, history of motion sickness, previous surgery and PONV.Patients were instructed to remain nil orally after 10 PM on the previous night of surgery.

Every effort was made to standardize the anesthetic technique. General anesthesia with controlled ventilation was used in all patients. Preoperative pulse rate, blood pressure and peripheral oxygen saturation were recorded in the operation theatre after connecting the following monitors:

1. Continuous electrocardiogram 2. Sphygmomanometer 3. Pulse oximeter

Peripheral venous access was established and intravenous fluid was started. The patients were premedicated with Inj. Glycolpyrolate 0.004mg/kg, Inj. Midazolam 0.2mg/kg, Fentanyl 2mcg/kg, all through intravenous routes, just before induction as patients were preoxygenated for 3 minutes before induction of anesthesia with Inj. Propofol 2 mg/kg. Inj. Succinylcholine 2mg/kg was used as muscle relaxant for intubation with appropriate size endotracheal tube. Inj. Vecuronium 0.08 mg/kg i.v.followed by one fifth of loading dose were used to provide muscle relaxation during surgery

Maintenance of anesthesia was with nitrous oxide (66%) and oxygen (33%) with Sevoflurane (0.5-1%) using controlled ventilation through closed circuit to maintain an $ETCO_2$ of 30-35 mm Hg. Patients were monitored during anesthesia using continuous ECG, heart rate, blood pressure, $ETCO_2$and pulse oximetry. 30 minute before the completion of surgery, antiemetic medication was administered. On completion of surgery, the residual paralysis was reversed with Inj. Neostigmine 0.05 mg/kg i.v.andGlycolpyrolate0.008 mg/kg i.v.and after complete recovery patients were extubated. Patients were transported to the recovery room and later to the ward after confirming an adequate level of consciousness and intact reflexes. The patients were observed for 24 hrs.postoperatively for nausea, retching and vomiting. Rescue antiemetic were given if vomiting occurred more than once, for nausea lasting more than 10 minutes or
at patient's request. Inj. Diclofenac 1.5 mg/kg i.m., were administered to patients who complained of pain.

The incidences of PONV were recorded within the first 24 hours after surgery at intervals of 0-6 hours, and 24 hours. Episodes of PONV were identified by spontaneous complaints by the patients or by direct questioning. ncidence of nausea and vomiting occurring in first six hours is considered as early nausea and vomiting and incidence of PONV after six hours was considered as late emetic episode.

"Complete response" was defined as the absence of nausea, retching or vomiting and no need for rescue antiemetic during the 24-hour observation period. Rescue antiemetic was provided with Inj. Metoclopramide 10mg i.v.in the event of 1 or more episodes of vomiting depending on the observer's discretion.

We made no distinction between vomiting and retching (ie., retching event was considered a vomiting event). Nausea and vomiting were evaluated on three-point ordinal scale. 0 = none, 1 = nausea, 2 = retching or vomiting.The incidence of nausea and vomiting in the two different groups was analyzed using Chi-square test, $p<0.05$ was considered significant.

RESULTS

A total number of 50 cases were taken into study. 25 of them received Palonosetron 0.075 mg, and the other 25 patients received Ondansetron 8mg for preventing postoperative nausea and vomiting through a period of 24 hours. All the patients completed the study. There were no statistically significant differences between the groups with respect to patient characteristics, type of surgery and duration of anesthesia. (Table-1)

The incidence of postoperative nausea and vomiting in 24-hour period was 12% and 48% in Palonosetron and Ondansetron respectively. (Table 2 chi-square = 7.8095, d*f* = 1; P (0.01) =6.63).The incidence of retching/vomiting in first 24 hours' postoperative period was 32% in Ondansetron group and no such episodes occurred with Palonosetron. (Table 2-chi-square = 9.6726; d*f*=1, P (0.01) = 6.63).Incidence of early nausea (0-6 hours) in Palonosetron and Ondansetron were 4% and 20% which was statistically insignificant (p value >0.05, table 3) whereas late nausea (6 – 24 hours) is 12% and 40% respectively which was statistically significant. (P value <0.05, table 3).

It was observed that 2 patients in Ondansetron and none in Palonosetron had vomiting during first 6 hours of postoperative period. There were no statistically significant differenc-

Patient characteristics	Mean Group A	Mean Group B	SD Group A	SD Group B	p value
Age	40.5200	39.8400	8.7088	7.4424	0.2968 NS
Weight	50.3600	48.1600	5.8158	6.7186	1.2379 NS
Duration of anesthesia (min)	100.0000	89.0000	26.6145	23.6291	1.5454 NS
Duration of surgery (min)	91.2000	99.2000	17.3973	25.1529	1.3079 NS
Group A – Palonosetron; Group B – Ondansetron					

Table-1: Demographic and anesthetic data

PONV	Group A (Palonosetron)	Group B (Ondansetron)
Present	3 (12%)	12 (48%)
Absent	22 (88%)	13 (52%)
Total	25	25

Table-2: Incidence of postoperative nausea and vomiting (ponv) in first 24 hours

	Palonosetron		Ondansetron	
Nausea	Early	Late	Early	Late
Present	1	3	5	11
Absent	24	22	20	14
Total	25	25	25	25

Table-3: Incidence of early nausea(0-6 hours) and late nausea (6-24 hours)

Vomiting	Palonosetron		Ondansetron	
Present	Early	Late	Early	Late
	0	0	2	8
Absent	25	25	23	17
Total	25	25	25	25

Table-4: Incidence of early (0-6 hours) and late (6-24hours) vomiting

es between the two groups (p >0.05 Table-4). There were no emetic episodes during 6-24 hours' postoperative period in Palonosetron group whereas 32% of patients in Ondansetron group developed emesis during this late postoperative period, which showed statistically significant difference (p<0.05 Table 4).

The incidence of postoperative nausea and vomiting in 24 hours' period was 12% and 48% in group A and Group B respectively.Chi Square = 7.8095, Degree of freedom = 1, P (0.01) = 6.63 (Table value of X2 at 0.01 level of significance).The incidence of nausea in first 24 hours of postoperative period was significant in Group B compared to Group A.Chi Square = 7.8095, degree of freedom = 1, P (0.01) = 6.63. (Table value of X2 at level of significance).

*Incidence of vomiting in first 24 hours of Postoperative Period:*There were no emetic episodes in Group A.Incidence of emetic episodes in Group B is 32%.Incidence of emetic episodes in 24 hours of postoperative period is significantly high in group B compared to group A (p <0.01).Chi square = 9.6726, degree of freedom = 1, P (0.01) =6.63. (Table value of X2 at 0.01 level of significance).

Incidence of early nausea (0-6 hours) in Palonosetron group and Ondansetron groups did not show any statistically significant difference. (P value >0.05).Chi-square = 3.219, degree of freedom = 1, P value (0.05) = 3.84. (Table value of X2 at 0.05 level of significance).

Incidence of late nausea was 12% and 40% in Ondansetron and Palonosetron groups respectively, which was statistically significant difference.Chi square = 5.1975, degree of freedom = 1, P value (0.05) = 3.84(Table value of X2 at 0.05 level of significance.

Both Palonosetron and Ondansetron were equally efficacious in preventing vomiting during early postoperative period after recovering from anesthesia (p value >0.05).Chi square = 2.602, degree of freedom = 1, P value (0.05) =3.84 (Table value of X2 at 0.05 level of significance).There were no emetic episodes during 6-24 hrs. postoperative period in Palonosetron group whereas 32% of patients in Ondansetron group developed emesis during this late postoperative period, which showed statistically significant difference.Chi square = 9.6726, degree of freedom=1, P value (0.05) = 6.63. (Table value of X2 at 0.05 level of significance).

DISCUSSION

In spite of so many advances in the management of postoperative nausea and vomiting with the invention of new drugs, multimodal approaches of management like administering multiple different antiemetic medication, less emetogenic anesthetic techniques, adequate intravenous hydration, adequate pain control, etc., the incidence of postoperative nausea and vomiting remains still high ranging from 25%-55% following inpatient surgery and 8%-47% following outpatient surgery.

Unfortunately, commonly used medications like antihistamines, anticholinergics, gastroprokinetic, butyrophenones, can cause undesirable side effects like sedation, dysphoria, restlessness and extrapyramidal symptoms. To overcome these, serotonin antagonists like Ondansetron, Tropisetron, Dolasetron, Granisetron, Ramosetron and Palonosetron were introduced for treatment of nausea and vomiting. They were primarily used in treating chemotherapy induced vomiting with minimal and clinically acceptable side effects. We compared most commonly used antiemetic Ondansetron with its newer congener, Palonosetron, a promising addition to the world of antiemetic.

In the present study, the antiemetic efficacy of Ondansetron and Palonosetron were assessed in first 24 hoursof postoperative period divided into two groups of assessment period (0-6 hrs., early postoperative period and 6-24 hours, late postoperative period) to assess the efficacy of both the drugs during different time intervals. We have selected similar groups of patients in respect of age, weight, duration of surgery and duration of anesthesia to compare the efficacy of the drugs. Analgesia for postoperative pain was standardized

and patients of both groups were observed for a period of 24 hours postoperatively. Hence we believe that the difference in postoperative nausea and vomiting is attributed exclusively to the study drugs.

Unlike Kim et al (2009), we have not included the placebo group in our study for want of approval from hospital ethics committee as the incidence of postoperative nausea and vomiting is very high in our set up without prophylactic antiemetic.

Although Ondansetron 4 or 8 mg has been recommended for preventing PONV, the meta-analysis by Ryu et al suggested that an 8 mg dose of Ondansetron was optimal for prevention of PONV. Therefore, Ondansetron 8 mg was chosen for this study. Palonosetron is a newly developed 5HT3 receptors antagonist with a more potent and longer receptor antagonizing effect compared with older 5HT3 receptors antagonists. In addition, the elimination half-life of Palonosetron is (40h). According to Park SK, Cho EJ, Kang SH, Lee YJ, Kim DA.Palonosetron is effective in preventing PONV after gynecological laparoscopic surgery and Palonosetron 0.075mg is an effective dose for preventing PONV.The manufacture's recommended dose is 0.075mg i.v.once a day. Therefore, Palonosetron at 0.075 mg dose was chosen for this study.[11]

Our study agrees with and confirms the various aspects of the above studies in most of the aspects. We found that Palonosetron has a definite advantage over Ondansetron in the prevention and treatment of postoperative nausea and vomiting in patients following laparoscopic surgery under general anesthesia. There was absolutely negligible need for rescue antiemetic medication in Palonosetron group whereas some patients in Ondansetron group needed rescue antiemetic medication in the form of Metoclopramide.

Kim SH et al. compared the anti-emetic efficacy of Palonosetron with ondansetron or ramosetron in high-risk patients undergoing laparoscopic surgery. They reported that the overall incidence of nausea/retching/vomiting was lower in the Palonosetron (22.2%/11.1%/5.6%) than in the ondansetron (77.1%/48.6%/28.6%) and ramosetron (60.5%/28.9%/18.4%) groups. The rescue antiemetic therapy was required less frequently in the Palonosetron group than the other groups ($P < 0.001$). Kaplan-Meier analysis showed that the order of prophylactic efficacy in delaying the interval to use of a rescue emetic was Palonosetron, ramosetron, and ondansetron. Our study confirmed the above.[12]

The study was conducted only in elective surgeries in patients with no obvious causes for nausea and vomiting. Patients with risk factors for post-operative nausea and vomiting like motion sickness, migraine and gastroesophageal reflux disease etc. were excluded from the present study. We decided to give the antiemetic medication towards the end of the surgery, 30 minutes before extubation.

CONCLUSION

Nausea and vomiting during post-operative period (within 6 hours after recovery from anesthesia) were effectively controlled with administration of Ondansetron and Palonosetron 30 minutes before recovery. Postoperative nausea and vomiting in the 6-24 hours' postoperative period after recovering from anesthesia was significantly lower with Palonosetron when compared to Ondansetron. (p value <0.01)

There were no statistically significant differences between the groups with respect to patient characteristics, type of surgery and duration of anesthesia.The postoperative sequelae, side effects and behavior of the patients, though not a part of our study were comparable in both the groups and both the drugs are safe for routine clinical use during laparoscopic procedures under general anesthesia.

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