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EFFECTS OF ONDANSETRON AND PALONOSETRON ON PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC SURGERIES: A COMPARATIVE STUDY

Anesthesiology

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ABSTRACT

Randomized blind study was carried out in 60 patients aged 18-65 ASA grade I & II, scheduled for elective Laparoscopic surgeries under general anaesthesia.

Patients were randomly allotted in 2 groups comprising 30 patients each. Group A: received Ondansetron (0.1 mg/kg)

Group B: received Palonosetron (0.075 mg)

After arrival to the operation theatre baseline monitoring- pulse blood pressure, ECG, SPO_2 observed & recorded. Intravenous line was secured. All patients were premedicated. Then Ondansetron or Palonosetron were given according to the group selection. After pre-oxygenation, induction with inj Thiopentone 5-7 mg/kg & facilitating intubation inj Succinylcholine 2 mg/kg were given. Patients were intubated and maintained with O_2 & Sevoflurane and muscle relaxant.

Vital parameters like pulse, BP, SPO_2, ECG, $ETCO_2$ were monitored throughout the surgery.After adequate oropharyngeal and endotracheal suctioning patients were extubated. Patients were shifted to post anaesthesia care unit for further follow up & observation. In post operative period, patients were monitored for vitals, episodes of vomiting, severity of nausea, complete response, requirement of rescue antiemetic, adverse drug reaction during 0-6, 6-24 & 24-72 hrs duration.

KEYWORDS

Ondansetron,Palensetron,Nausea,Vomiting

INTRODUCTION

Post operative nausea and vomiting (PONV) is an unpleasant experience that affects 20-30% of surgical patients after general anaesthesia.[13]It decreases patient comfort and cause prolonged hospital admission.It may cause dehydration, electrolyte imbalance, and aspiration of gastric contents, oesophageal rupture, suture dehiscence and bleeding. It is a multifactorial phenomenon that can be triggered by multiple receptor pathways at peripheral, central or both sites. Various patient factors,surgical factors, anaesthesia related factors increases the incidence of PONV.

Laparoscopy is a very popular technique used in various surgical procedures, done under general anaesthesia. It offers advantage of minimal surgical trauma, less intra operative and post operative pain, short recovery time and reduces the cost of hospital stay. The main problem associated is higher incidence of PONV.

Anti-emetics are the main stay therapy for PONV.

The present study was conducted to evaluate the effects of Ondansetron and Palonosetron on prevention of post operative nausea and vomiting in patient undergoing laparoscopic surgeries.

The nausea and vomiting response is regulated by the vomiting centre in the brain-stem. The various neurotransmitters involved in the regulation are: dopamine-2, serotonin, acetylcholine, histamine and substance P.The most important afferent routes for these factors are derived from

- Vagus nerve
- Chemoreceptor trigger zone
- Labyrinth
- Higher cortical centres

Ondansetron

It is a specific serotonin receptor ($5HT_3$) inhibitor.It has a relatively short half life (3–5 hours) and undergoes extensive liver metabolism.. The antiemetic effect of Ondansetron is better than its anti nausea efficacy. It is most effective when given at end of surgery.Ondansetron prevents vomiting more effectively in children.

Dose:

- 0.15mg/kg orally
- 0.05 to 0.15mg/kg IV .

The recommended dose for prophylaxis is 4 to 8 mg I.V.in adults and 50 to 100µg/kg in children.

Headache, diarrhea, transient increases liver transaminases, cardiac arrhythmia and conduction disturbance, myocardial depression, prolonged QT interval are the side effects.

PALONOSETRON

Palonosetron is a “second generation”5HT3-RA.It has the highest binding affinity to the 5-HT3 receptor and at approximately 40 hours the longest elimination half life Unlike the representatives of the first generation with competitive inhibition of the 5-HT3 receptor, Palonosetron seems to exhibit allosteric binding and positive cooperativity leading to effects persisting beyond the mere receptor binding time.52The metabolism of Palonosetron is primarily in the liver The slow elimination of palonosetron results in a long terminal half-life of approximately 40 hours,which contrasts with Ondansetron (3–5 hours)

High receptor affinity is accompanied by high selectivity for other receptors which makes it unlikely that Palonosetron will produce unwanted effects at other receptor sites.

Dosage and administration

For PONV:Adults – a single 0.075 mg I.V. dose administered over 10 seconds immediately before the induction of anesthesia.

Adverse reactions

Transient headache (9%), QTc prolongation, sinus bradycardia, tachycardia, hypotension,pruritusflatulence, upper abdominal pain, salivary hypersecretion, dyspepsia, diarrhea, intestinal hypomotility, anorexia,Constipation

MATERIAL AND METHODS

After approval from Ethics Committee & informed written consent from the patients, single blinded randomized study of observational type was carried out in 60 patients aged 18-65 ASA grade I & II.

Patients were randomly allotted in 2 groups comprising 30 patients each. Group A: received Ondansetron (0.1 mg/kg)
Group B: received Palonosetron (0.075 mg)

After arrival to the operation theatre baseline monitoring- pulse blood pressure, ECG, SPO2 observed & recorded. Intravenous line was secured. All patients were premedicated with inj. Glycopyrrolate 0.004 mg/kg and inj Fentanyl 1-2 ug/kg iv. Then Ondansetron or Palonosetron were given according to the group selection. After pre-oxygenation, induction with inj Thiopentone 5-7 mg/kg & for facilitating intubation inj Succinylcholine 2 mg/kg were given. Patients were intubated and were maintained with O2 & Sevoflurane and muscle relaxant.

Intraoperative Pulse,BP, SPO2, ECG, ETCO2 were monitored and documented till the end of surgery. After completion of surgery, neuromuscular blockade was reversed with Inj. Glycopyrrolate 0008 mg/kg & Inj Neostigine 0.05 mg/kg i.v. After adequate oropharyngeal and endotracheal suctioning patients were extubated. Patients were shifted to post anaesthesia care unit for further follow up & observation. In post operative period, patients were monitored for vitals, episodes of vomiting, severity of nausea, complete response, requirement of rescue antiemetic, adverse drug reaction during 0-6, 6-24 & 24-72 hrs duration.

Continuous data were expressed as mean & SD univariate analysis. Univariate analysis of continuous data was performed using chi-square test or through a student's t-test. Level of significance was accepted at $p<0.05$. Statistical data were analysed by using SPSS version 22 software.

OBSERVATION AND RESULTS

Comparative study between use of Ondansetron and Palonosetron to prevent post operative nausea and vomiting was done among 60 patients of either sex undergoing laparoscopic surgeries under general anaesthesia. The following observation and results were recorded.

TABLE 1: PONV Score

		Group A (n=30)	Group B (n=30)	P value
0-6 hrs	Nausea	07 (23.33%)	3 (10.00%)	0.1265
	Vomiting	02 (06.66%)	0 (0)	0.4720
	PONV	09 (33.33%)	3 (10.00%)	0.1066
6-24 hrs	Nausea	10 (33.33%)	2 (06.66%)	**0.0239**
	Vomiting	04 (13.33%)	1 (03.33%)	0.3502
	PONV	14 (46.66%)	3 (10.00%)	**0.0042**
24-72 hrs	Nausea	10 (33.33%)	5 (16.66%)	0.9772
	Vomiting	05 (16.66%)	4 (13.33%)	0.4989
	PONV	15 (50.00%)	9 (30.00%)	0.1876

Table 1 shows the PONV score at various time interval.Nausea and vomiting were evaluated by **PONV SCORE** which was assigned as, 0-complete response, 1-nausea, 2- vomiting, 3-rescue antiemetic given (Inj Metoclopramide 10 mg i.v.)

Inference: The number of patients with PONV Score:
In 0-6 hrs, both groups were comparable while during 6-24 hrs is significantly higher in Group A as compare to Group B. The difference is mainly due to the difference in number of patients having nausea (33.33% vs 6.66%), while number of patients having vomiting is comparable in both groups. In 24-72 hrs both groups were comparable

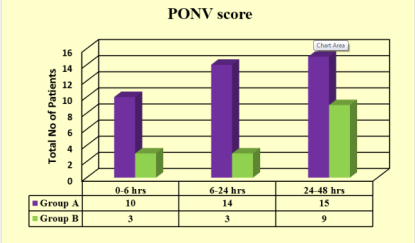


FIGURE 1:

This graph shows the PONV score at various time interval in both groups.

TABLE 2: Incidence of Vomiting

	Group A (n=30)	Group B (n=30)	P value
0-6 hrs	02 (6.66%)	00 (00.00%)	0.4720
6-24 hrs	04 (13.33%)	01 (3.33%)	0.3520
24-48 hrs	05 (16.66%)	04 (13.33%)	1.0000

Table 2 shows patients experiencing vomiting in two groups at different time interval which was not statistically significant

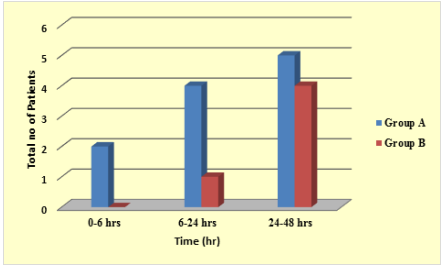


FIGURE 2:

This graph shows the patients experiencing vomiting in two groups at different time interval

TABLE 3: Complete Response

Complete Response Time (hrs)	Group A (n=30)	Group B (n=30)	P Values
(0-6 hr)	21 (70%)	27 (90%)	0.1066
(6-24hr)	16 (53.3%)	27 (90%)	**0.0042**
(24-72hr)	15 (50%)	21 (70%)	0.1876

Table 3 shows the comparison of complete response in both the groups

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Inference:
0-6 hrs: were comparable in both groups
6-24 hrs is significantly lower in Group A as compare to Group B. (53.33% vs 90%).
24-72 hrs were comparable in both groups

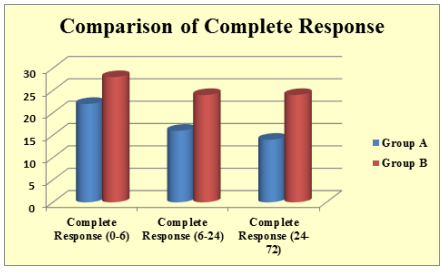


FIGURE 3:

Graph shows the comparison of complete response in both the groups at various time intervals.

TABLE 4: Complications and Adverse Effects

Drug	Group A	Group B	P value
Headache	4(13.3)	2(6.7)	0.6670
Dizziness	3(10)	1(3.33)	0.6048
Gastritis	1(3.33)	1(3.33)	0.4720
Rashes	0	0	0

The above table shows the incidence of complaints in post operative period.

DISCUSSION

Postoperative nausea and vomiting (PONV) is a common problem in the general patient population, occurring in an estimated 20-30% of all patients. It may lead to significant morbidity from dehydration, electrolyte imbalance, and aspiration of vomiting. Surgical complication like wound dehiscence, bleeding beneath skin flaps and loss of vitreous fluid following intraocular surgery may follow severe PONV. [23, 27] The etiology and subsequent consequences of PONV are

complex and multi-factorial.. Various therapeutic preventive measures are known to influence the incidence of PONV.

Laparoscopic surgeries are done very commonly nowadays in every part of the world.These surgeries usually done under general anaesthesia, represent a highly susceptible group for occurrence of PONV with both anaesthetic and non-anaesthetic factors contributing to the problem. Although the mechanism of PONV after laproscopy is unclear, it is postulated that it is due to stimulation of the vagal afferents on the bowel and peritoneum when the peritoneal cavity is inflated with CO_2 during laproscopy. Neurogenic pathways are activated by traction reflexes, by splanchnic pressure and manipulation may lead to PONV.The newer class of antiemetics used for prevention and treatment of PONV are 5-HT3 receptor antagonist. The mechanisms of actions are both central and peripheral. It blocks the 5HT-3 receptors in the area postrema, nucleus tractus solitarious and adjacent areas of brain which are related to nausea and vomiting. Also, it blocks 5HT-3 receptors in the mucosal vagal afferents in the GIT.[8,10] Ondansetron is a selective 5-HT3 receptor antagonist. It is 1st one of this group, having shorter duration of action. Palonosetron is newer 2nd generation 5HT-3 receptor binding agent having the highest binding affinity to the 5HT-3 receptors. It has longer duration of action. It seems to exhibit allosteric binding and positive cooperativity leading to effects persisting beyond the receptor binding time[10,21]

This study was planned to evaluate the clinical efficacy and safety of Palonosetron in patients undergoing laparoscopic surgeries and its comparison with Ondansetron.

Nausea and vomiting were evaluated by PONV SCORE which was assigned as 0 -Complete response, 1 - Nausea, 2 - Vomiting, 3 – 1st Rescue antiemetic required (Inj. Metoclopramide 10 mg i.v.) and it was observed at different time interval.

In 0-6 hrs time interval, incidence of nausea and vomiting was 10% and 0% respectively in Palonosetron group while it was 23.33% and 6.66% respectively in Ondansetron group. The PONV score was 10% in Palonosetron while it was 33.33% in Ondansetron group. The results were comparable in both groups which was statistically not significant (P value - 0.1066)

In 6-24 hrs time intervals, incidence of nausea and vomiting was less with Palonosetron as compared to Ondansetron It was 6.66% and 3.33% respectively in Palonosetron group while it was 33.33% and 13.33% respectively in Ondansetron group. The PONV score was significantly lower in Palonosetron group i.e. 10% as compared to Ondansetron group which was 46.66%. PONV score was significantly higher in Group Ondansetron as compare to Group Palonosetron (P value-0.0042.

In 24-72 hrs time interval, incidence of nausea and vomiting was 16.66% and 13.33% respectively in Palonosetron group while it was 33.33% and 16.66% in Ondansetron group. The PONV score was 30% in Palonosetron while it was 50% in Ondansetron group. The results were comparable in both groups and statistically not significant (P value - 0.1876). Though overall PONV score and incidence of nausea-vomiting is less with Palonosetron, the results were statistically not significant. Palonosetron was more effective during 6-24 hr time interval.

This proves the effectiveness of both drugs in preventing the emesis in postoperative period.. Palonosetron exhibits highest receptor affinity and longer half life that confers a prolonged duration of action as compared to ondansetron.

SUMMARY AND CONCLUSION

After the study, following conclusions were made:

1) Palonosetron was highly effective in preventing post-operative nausea and vomiting particularly in the 1st 24 postoperative hours as compared to Ondansetron.
2) Complete response of drug was significantly higher in Palonosetron group during 1st 24 hours as compared to Ondansetron group.
3) Both Palonosetron and Ondansetron were safe. No adverse effects of clinical significance were observed and All the patients were hemodynamically stable in both the groups.

So to conclude, Palonosetron 0.075 mg is very effective and long lasting in prevention of post-operative nausea and vomiting as compared to Ondansetron in the patients undergoing laparoscopic surgeries under general anaesthesia.

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