

Comparison of palonosetron with ondansetron for preventing post operative nausea and vomiting in patients undergoing abdominal surgeries under general anaesthesia - A comparative Observational study

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Abstract

Background and Aims: Postoperative nausea and vomiting (PONV) is a known complication in surgery under General anesthesia. In order to identify surgical patients who may benefit from prophylactic antiemetic medication to prevent Postoperative nausea and vomiting, by using a simple ten point VAS (Visual Analogue score) and four point VDS (Verbal descriptive scale) scoring system in terms of severity of nausea and vomiting -mild, moderate and severe. There are many antiemetic drugs in use for prevention of PONV. Palonosetron is new entrant with longer duration of action. We decided to compare the efficacy of intravenous administered palonosetron versus ondansetron in terms of severity of nausea and vomiting in 60 patients of ASA Grade I&II undergoing abdominal surgery under general anaesthesia in long term prevention of PONV and observations of incidence of changes in Haemodynamic status, adverse reactions, complete response, need of use of rescue antiemetic treatment and overall patient's satisfaction. **Methods:** Observational study was conducted to compare efficacy and safety of intravenous Palonosetron 0.075 mg and ondansetron 8 mg single dose given prophylactically for prevention of PONV. All data were statistically analysed and incidence and severity of vomiting episodes and nausea were recorded with visual analog scale (VAS) > 4 were evaluated at 0-2 hours, 2-6 hours, 6-12 hours, 12-24 hours and 0-24 hours in post operative period by using VDS scoring system after injection of study drugs. In a prospective study, 60 patients posted for various types of abdominal surgeries under general anaesthesia. Inj. Metoclopramide 10 mg was given as rescue medication when VAS was more than 4. **Results:** Patients easily understood both VAS and VDS numeric scoring system, overall incidence of nausea and vomiting was less in group palonosetron than ondansetron and numbers of patients were more requiring rescue medication in ondansetron group and adverse reactions were also less in group P than O. There was no significant difference in haemodynamic status in both groups. Overall patients satisfaction was comparable in both groups. **Conclusion:** observational study concluded that prophylactically use of palonosetron 0.075 mg is more effective than 8 mg of ondansetron for prevention of PONV in abdominal surgeries under general anaesthesia.

Key Words: Palonosetron, Ondansetron, Post Operative Nausea vomiting, Abdominal surgeries Comparative study.

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The Post Operative Nausea and Vomiting (PONV) is a very common unpleasant feature and big problem, rather a challenge during and after general anaesthesia, almost in all abdominal surgeries including laparoscopic surgeries¹. There can be high level of discomfort after surgery. It can be very distressing and can sometimes result in dehydration, gastric aspiration, wound dehiscence, Post Operative Nausea and Vomiting if associated with post operative pain can be more dangerous. Nausea is defined as subjective unpleasant sensation

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associated with urge to vomit where as vomiting is forceful expulsion of gastric contents from the mouth and retching is labored, spasmodic rhythmic contractions of respiratory muscles without expulsion of gastric contents.²

PONV can occur immediately after reversal of anaesthesia and incidence is more during first 24 hours and highest after abdominal surgeries³. Many factors influence PONV like age, sex, opioid administration, suctioning, anaesthetic drugs, upper abdominal surgeries etc.^{3,4}. In high risk cases incidence can be as high as 80% indicating importance of management of vomiting and nausea during and after surgery. Laparoscopic surgery is one condition where risk of PONV is high^{1,2,3,4}. PONV can occur after commencement of surgical procedure or beyond also^{2,5}. It is believed during laparoscopic surgeries there is pressure on vagus nerve due to pneumoperitoneum can cause PONV,^{3,4} It may cause serious complications like dehydration, electrolyte imbalance, disruption of surgical repair thereby increasing cost of therapy^{3,4,6,7}. A number of drugs have been tried for prevention of PONV like Antihistaminic, Butyrophenol and Dopamine receptor antagonist but there are many side effects like excessive sedation, hypertension, dysphoria, hallucination, extra pyramidal symptoms but so far as no claim can be made for any drug for excellent results^{5,6}. 5 HT₃ receptor antagonists have been used for last 25 years and produced less side effects. Inj. Metoclopramide 10 mg has been in use for many decades but was in-effective. Inj. Ondansetron is also being widely used for Intra operative and Post operative period. Now newer 5HT₃ receptor antagonist drugs like Inj. Palonosetron and Granisetron, Dolasetron, Tropisetron, Romasetron as anti emetic agents have been introduced and have been tried with minimum side effects and are being compared⁷. Now a days with the invention of new drugs having more efficacy over Ondansetron and Metoclopramide and effective for longer duration of time. we decided to conduct this present study where we compared efficacy of Palonosetron with Ondansetron. Inj. Palonosetron is selective serotonin subtype 3 (5 HT₃) receptor blocker of dose 0.075 mg is effective and it is claimed by many authors that effect remains for 24 hours with single dose where as Ondansetron 8 mg intravenously remains effective for 3 to 5 hours only and we have add to any other antiemetic agent as rescue medication again if there was incidence of PONV, Considering some of these proposed advantages to test this hypothesis, we conducted this observational study.

Inclusion criteria and informed consent Informed consent was taken and procedure was explained in details to each and every patient. Before induction of general anaesthesia undergoing for elective abdominal surgeries. All cases of ASA Grade I and II were selected for study assessment for PONV.

Exclusion criteria Non consenting patient, Patients with any previous history of hypersensitivity or any known side effect of Antiemetic drugs. Pregnancy and Lactation., Menstruating women. Administration of any anti psychotic drugs, steroids within 24 hours before surgery, Presence of any respiratory or CVS Disease, Obesity (body mass more than 35) was excluded from study.

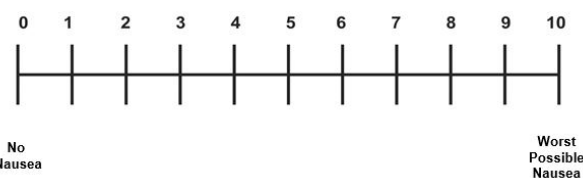
Material and Methods After getting the clearance from Institutional Ethics Committee (IEC), In this observational study 60 ASA I and II patients in the age of 18 to 75 years undergoing for all types of abdominal surgeries under general anaesthesia were allocated to two groups alternatively. Group A Inj. Palonosetron 1.5 ml of 0.075 mg and Normal Saline 0.5 ml was added to make it 2 ml and Group B Inj. Ondansetron 8 mg of 2 ml both the anti ametic drugs were given intravenously. before induction of General Anaesthesia.. The services of other Anesthesiologists and staff nurses on were utilized in post operative period.

Induction In both groups after keeping patients fasting as per protocol and Tablet Ranitidine 150 mg, Tab. Alprazolam 0.25 mg in the night and after premedication Inj. Butorphenol 1mg, Inj. Midazolam 1 mg (0.05mg per kg), Inj. Glycopyrrolate 0.2 mg (0.004Mg per Kg) half hour before surgery, Induction was carried out with Inj. Propofol 2 mg / kg and Inj. Scoline 2 mg /kg. After achieving endo tracheal intubation with appropriate size of Endotracheal tubes, Maintenance was carried out by using mixture of Oxygen and nitrous oxide in 1:2 ratio with Isoflurane in the concentration 0.5% to 1% and muscle relaxant like Inj. Vecuronium bromide as per requirement.

Monitoring Monitoring were started from the point the patient arrives in OR. The parameters monitored were as follows Pulse, NIBP, Blood loss, Oxygen Saturation (Sao₂), ETCO₂, Urine Output, any other untoward events or any complication were strictly monitored and recorded. Hemodynamic parameters were recorded before induction to Post Operative period in recovery and up to 24 hours when patient was shifted to ward, Duration of action were recorded and calculated from first dose of anti emetic agents first two hours, then 2-6 hours, 6-12 hours and 12 to 24 and 0-24 hours for frequency of episode for Nausea and Vomiting. Appropriate distribution of demographic data like age, sex, body weight, Duration and category of surgery. Specifically designed Nausea and Vomiting scoring system were used for assessment of incidence of PONV and this scale has been developed by authors, which has been already published.^{8,10} Numeric four point VDS (verbal descriptive scale) PONV scoring System was used Score as (zero) 0 - No Nausea or vomiting, 1- Mild Nausea means sometimes, Score 2- Moderate Nausea means often or most of times and score 3 means severe nausea all the times 3- Severe Nausea 4 –

Retching / vomiting.^{10,11} In this study classical VAS scale was also used for observing nausea (0-10 cm) 0-1 no nausea and 1⁺-4 mild nausea, 4⁺-7 moderate nausea and 7⁺-10 severe nausea score was used.¹¹ They have further described Vomiting score as no vomiting score 0 (zero), episode of vomiting once or twice score 1 and multiple vomiting score 2 in post operative period. At the end of study adverse reactions like Headache, Dizziness, Drowsiness, Bradycardia, Hypertension, Prurities, Seizure if any were recorded. Requirement of rescue Medication in both groups were recorded. Patients satisfaction were recorded as Highly Satisfied, Satisfied, Neutral, Dis-Satisfied. VAS Nausea Scale of 10 cm given below was recorded as per patients observation. The Post operative nausea and vomiting (PONV) is a very common unpleasant feature and big problem rather a challenge after General as well as regional especially spinal and epidural anaesthesia in almost all abdominal surgeries including laparoscopic surgeries. There can be high level discomfort after surgery. It can be very distressing and can sometimes result in dehydration, gastric aspiration wound dehiscence. PONV if associated with post operative pain can be more dangerous. Nausea is defined as subjectively unpleasant sensation associated with urge to vomit whereas vomiting is if forceful contents of gastric contents from the mouth or retching (labored, spasmodic rhythmic contractions of respiratory muscles without expulsion of gastric contents). PONV can occur immediately after reversal of anaesthesia and incidences are more during first 24 hours and highest after abdominal surgeries. Many factors influence PONV like age, sex, opiate administration, suctioning, anaesthetic drugs, upper abdominal surgeries etc. In high risk cases incidence can be as high as 80% indicating importance of management of vomiting and nausea during and after surgery. A number of drugs have been tried for prevention of PONV like Antihistaminics, Butyrophenone and Dopamine receptor antagonist but there are many side effects like excessive Sedation, Hypertension, Dysphoria, Hallucination, extra pyramidal symptoms but so far no claim can be made for any drug for excellent results. 5-HT₃ receptor antagonist has been in use for last 25 years and produced less side effects presently in this category. Inj Metoclopramide 4 mg has been in use for many decades used but was ineffective. Inj Ondansetron is also being widely used for PONV and other 5HT₃ receptor newer

drugs like Inj. Palonosetron and Granisetron, Dolasetron, Tropisetron, Romisetron anti emetic agents have been tried with minimum side effects and is being compared. VAS Visual analog scale was widely used for observing nausea and vomiting. V=0 means no vomiting and 10 means worst vomiting or nausea now a days. With the invention of new drugs having more efficacy over ondansetron and metoclopramide and effective for longer duration of time we decided to conduct present study and this is first study of Palonosetron at this institute and in this study prospective, randomized and double blinded study we will compare efficacy of Palonosetron with Ondansetron. Palonosetron is selective serotonin subtype 3 (5-HT₃) receptor antagonist dose 0.075 mg and effect remains for 24 hours with single dose whereas Ondansetron 8 mg intravenously remains effective for only 3 to 5 hours.



Rescue medication Inj. Metoclopramide 10 mg were given if episode of Nausea and Vomiting during surgeries and in post operative period

Statistical analysis

The data collected from this prospective, observational study were entered into a master chart and necessary statistical tables were constructed. The statistical constants like arithmetic mean, standard deviation, percentage etc. were computed to get valid inference about the data for comparison. In order to see whether the difference in estimates in the study groups are statistically significant, the students unpaired 't' test and Fischer's exact proportions were applied. Individual unpaired t test were applied for comparison of post operative hemodynamic parameters and the results were analyzed using ANOVA test for comparison between groups and within groups. A P value of less than 0.05 was considered statistically significant. A p value 0.05 to 0.10 was significant and more than 0.01 ≤ 0.05 was considered as moderately significant and p value ≤ 0.01 was considered as strongly significant.

RESULTS

This study was conducted with 60 ASA Grade I & II all adults of age 18 to 75 years of age fixed for elective surgeries under General anaesthesia. Specially designed Nausea and Vomiting scoring system used for assessment of incidence of PONV 0 - No Nausea 1- Mild Nausea 2- Moderate Nausea 3- Severe Nausea 4 -Retching / Vomiting.

Table 1: Demographic Profile Distribution of age , weight ,HR , Mean BP , Duration of surgeries

	Group1 Palonosetron n=30	Group 2 Ondansetron n=30
Age	42.2(±10.2)	41.5(±11.5)
Sex /Gender	18 Male (60%) 12 Female (40%)	17 Male (56.6%) 13 Female (43.4%)
Weight	58.23(±5.52)	56.62(±5.32)
Mean HR	72.34 (±8.32)	74.76(8.23±)
Mean MAP	78.76(±3.86)	81.42(±4.72)
Duration of surgeries(min)	107.4(±15.18)	103.4(±16.11)
ASA Grade1	22 (73.3%)	23(76.6%)
ASA Grade 2	8(26.6%)	7(23.3%)

Table 2: Severity of ponv on the basis of VAS score and episodes of vomiting

Variable	Severity (Episodes of Vomiting)	Number of Patients (N=30)
Nausea	Mild (1-4)	18 (60%)
	Moderate (4-7)	08 (27%)
	Severe (>7)	04 (13%)
Vomiting	Mild(1)	15 (50%)
	Moderate (2)	10 (33%)
	Severe (>2)	05 (17%)

Table 3: Verbal descriptive scale (VDS)

Period	PONV Score 0 to 4	Group 1 Palono setron n=30	Group 2 Ondan setron N=30
0-2 hours	Score 0	20 (66.66%)	16(53.33%)
	Score 1	4 (11.11%)	3(10%)
	Score 2	2(0.66%)	4(11.11%)
	Score 3	2(0.66%)	2(0.66%)
	Score 4	2(0.66%)	5 (16.66%)
2-6 hours	Score 0	24(80%)	16(53.33%)
	Score 1	2(0.66%)	2(0.66%)
	Score 2	1(0.33%)	3(10%)
	Score 3	1(0.33%)	5(16.66%)
	Score 4	2(0.66%)	4(11.11%)
6 -12hours	Score 0	24(80%)	18(60%)
	Score 1	2(6.66%)	5(16.66%)
	Score 2	2(6.66%)	4(11.11%)
	Score 3	1(0.33%)	2(0.66%)
	Score 4	1(0.33%)	1(0.33%)
12-24 hours	Score 0	24(80%)	18(60%)
	Score 1	4(11.11%)	4(11.11%)
	Score 2	00(00%)	3(10%)
	Score 3	00(00%)	1(0.33%)

P < 0.05 not significant

Table 4: Description of Incidence of PONV evaluation of 60 patients

Extent	PONV 0-2 hours	PONV 2-6 hours	PONV 6-12 hours	PONV 12-24 hours	PONV 0-24 hours
Actively Treated n (%)	9	6	3	0	18
Nausea pattern					
1.Varying	18	6	4	2	30
Constant n(%)	6	4	2	2	14
Nausea					
0No nausea	20	34	36	54	54
1Sometimes	13	7	4	4	2
2.Often/Most of times	10	5	7	4	1
3 All the times	17	7	6	4	0
Duration of Nausea Varying	19	8	4	2	0
Constant n(%)	7	6	7	0	0
Number of vomit n(%)					
1 time	1	0	0	0	1
2 times	1	0	0	0	0
3-and more times	0	0	0	0	0
Dry retching					
VAS more than 7 cm n (%)	0	1	0	0	0

P < 0.05 not significant**Table 5:** Incidence of complete response and rescue medication

Period	Response	Group1	Group 2
0-2 hours	Complete response	20 (66.66%)	16(53.33%)
	Rescue medication	3(10%)	10(33.33%)
2-6 hours	Complete response	24(80%)	16(53.33%)
	Rescue medication	5 (16.66%)	8(26.66%)
6-12 hours	Complete response	24(80%)	18(60%)
	Rescue medication	0	6(20%)
12 -24 hours	Complete response	24(80%)	18(60%)
	Rescue medication	2 (6.66%)	4(13.33%)
0 -24 hours	Complete response	24(80%)	15(50%)
	Rescue medication	6(20%)	12(40%)

Complete response was more in group P than O through out

Table 6: Incidence of adverse reactions

Adverse reaction/Response	Group 1 Palono setron n =30	Group 2 Ondan setron n=30
Dryness of mouth	1(3.33%)	2(6.66%)
Fatigue	0	2(6.66%)
Constipation	2(6.66%)	3(10%)
Allergic reactions	0	0
Respiratory distress	0	0
Hypertension	0	0
Bradycardia	0	1(3.33%)
Hypotension	0	0
Headache	3 (10%)	2(6.66%)
Dizziness	3 (10%)	4(13.33%)
Drowsiness	0	1(3.33%)
Total	8(26.6%)	15(50%)

Table 7: Patients Satisfaction Score

	Group1 Palonosetron n=30	Group 2 Ondan setron n=30
Highly Satisfied	15(50%)	8(26.66%)
Satisfied	8 (28.8%)	9(30%)
Neutral	5 (15%)	8 (26.66%)
Dissatisfied	2 (6.2%)	5(16.6%)

DISCUSSION

Post operative nausea and vomiting (PONV) is known serious complication in addition to post operative pain in most of surgeries under General Anaesthesia which is main cause of discomfort , uneasiness after surgeries . therapeutic use of anti emetic agents for PONV as in practice for many decades as they have less adverse effects^{9,10,11} . Incidence of PONV may be associated due to many factors like age , sex , prior history of smoking and motion sickness , inhalational gases and used in general anaesthesia .¹⁴ There are several factors which are involved in nausea and vomiting like 5HT₃ Receptors , Dopamine D₂, Histamine 2, α -Adrenergic , Muscarinic , Cholinergic , Neurokinin , GABA Receptors are involved in initiation of nausea and vomiting in post operative period . 5HT₃ RA`s are commonly used anti emetics after 1990`s to control PONV due to their efficacy and less risk factors and they block these receptors . PONV is due to stimulation of 5HT₃ receptors in gut in vagal afferent fibres and also centrally present in chemoreceptor trigger zone (CTZ) at the floor of 4th ventricle .CTZ

has affinity to vomiting centre in lateral reticular formation of medulla oblongata^{15,16} . The gut stimulation can be due to inhalational gases , opioids , distention of gut , irritants like swallowed secretions and blood .Similarly CTZ are stimulated due to inhalational gases. PONV is associated with various types of morbidities like inadequate fluid

intake , Dehydration , Pulmonary aspiration , Surgical site bleeding and wound dehiscence , Increased Post operative pain , Rarely Pneumothorax and Surgical Emphysema ,even oesophageal rupture have been reported¹⁹ . The use of antiemetic in PONV like . 5HT₃ RA`s have been proved to be more effective with minimum side effects or adverse reactions on vitals and longer duration of action , with no sedative effect. That Ondansetron has been proved to be more superior than Methylprednisolone and Metaclopramide for prevention of PONV . Ondansetron was first 5HT₃ RA and frequently being used for PONV and remained effective for 3 to 5 hours and more superior than Metaclopramide and Methylprednisolone in prevention for PONV . Palonosetron is second generation 5HT₃RA with comparatively reduced incidence of PONV in dose of 0.075 mg as reported by Kovac et al .¹⁵ Palonosetron has high affinity to selectivity to 5 HT₃ receptors and its PK 10 is 100 times more than Ondansetron and undergoes with slow elimination which results in longer half life of 40 hours as compared to Ondansetron which has half life of 3-5 hours hence shorter duration of action .^{15,16,17} study conducted by White and Scruden et al¹⁸ . different doses were tried 1ugm /kg to 30 ugHT₃ Palonosetron were used but found that minimum dose of 1 ug / kg is equally effective as 30 ug / kg as per white and Scruderi et al¹⁶ . Minimum effective dose has approved by FDA is 0.075 mg^{15,16} . Some studies already conducted are

of view for combination therapy than mono therapy of anti emetic drugs in high risk cases of PONV as it increases efficacy , reduction in dose , less side effects , longer duration of action as compared to single drug . In another study , combination of Granisetron 3 mg and Inj. Methylprednisolone 1.25 mg was more effective than single drug . Dexamethasone 8 mg combined with Ondansetron 8 mg was more effective than Ondansetron alone . Yet another study for PONV these results suggest Palonosetron combined with Dexamethasone is more effective and longer duration of action than Palonosetron used alone . However there is no study which suggest that Palonosetron can be used as rescue medicine in cases of Ondansetron proved ineffective in PONV . As per SAMBA guidelines , in cases of PONV , rescue medication be given different drug given prophylactically . if no anti emetics are prior to surgery 5HT₃ RA's are more effective. In our study Palonosetron 0.075 mg and Ondansetron 8 mg were given and their effects were compared and incidence of PONV were less in Palonosetron than Ondansetron group and it was observed that efficacy of Palonosetron is much more than Ondansetron . The Palonosetron is extensively used for prevention of chemotherapy induced nausea and vomiting . it has been approved by FDA for prophylaxis against PONV. Mechanism of action of Palonosetron is different from other 5HT₃RA's. Patient with more than VDS score 2 and VAS Score 4 were given rescue medication . In entire 24 hours assessment complete response were in more cases treated with Palonosetron and were less in cases treated with Ondansetron in 0- 24 hours . That rescue medication were required in less cases in Palonosetron group than of Ondansetron group As far as safety drugs ,both the drugs were well tolerated. That adverse reactions were comparatively less with Palonosetron than Ondansetron like constipation , Dizziness , Headache in the present study and 5HT₃RA's of less risk factors and more efficient . VDS (Verbal Descriptive Scale) Numeric scoring 0-4 and VAS (visual analogue scale) of 10 cm were used for PONV in this study^{17,18} and its severity were recorded by staff nurse under supervision of anaesthesiologist on duty . There have been many studies to create numeric score used for severity of PONV but till date no score or VAS has been validated to define severity of PONV and at what stage it becomes significant and antiemetic drugs are required. .Pattern of Nausea is also scored as constant or varying , In previous studies , Apfel scoring system though simple for PONV has extensively been used but it depends upon many factors like gender , Age , Motion sickness etc.²³ and there is no explanation for mild , moderate , severe nausea in this scoring system , but in our study , we emphasized for a scoring based on number of episodes of nausea and vomiting in VDS and VAS (Visual Analogue

Scale) of 10 cm line marked as no nausea on the left side of scale and severe nausea on the right side of scale at end 10 cm. nausea were described as lot less , A little less , the same , a little more , a lot more . A scale greater than 7 cm was considered as severe nausea and scale of less than 3 cm was considered as insignificant . Rescue medication Inj. Metoclopramide 10 mg was given when more than two episode of PONV occurred or in cases VAS more than 5 cm or VDS more than 2 reported.²⁰ All other measurements like adverse reactions , complete response , need for rescue medication were also recorded . it was observed that Palonosetron group required less rescue medication as compared to Ondansetron group who underwent surgeries There were no significant difference between two groups as regards Hemodynamic status , p Value ≥ 0.005

Conclusion;- Intravenous Palonosetron 0.075 mg is more effective , longer duration of action , less adverse reactions and less requirement of rescue anti emetic drugs than Ondansetron 8 mg in preventing PONV in surgeries under general anesthesia in period of 0-24 hours . Overall patient satisfaction , Complete response were more in Palonosetron group as compared to Ondansetron .

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