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Comparison of Ondansetron v/s Palonosetron for Prevention of Post-Operative Nausea and Vomiting in Laparoscopic Surgery.

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ABSTRACT

Postoperative nausea and vomiting (PONV) is the most common complication of surgery and anaesthesia, leading to adverse consequences including patient dissatisfaction, unexpected hospital admission, and delayed recovery and return to work. The present study was designed to evaluate the efficacy of Palonosetron compared with Ondansetron for preventing PONV in patients undergoing laparoscopic surgery. Randomized Double Blinded study. A total of 100 ASA class I-II patients scheduled for laparoscopic surgery under standardized general anaesthesia were randomly divided into two groups (n = 50 each). Group O patients were received ondansetron 4 mg i.v. and group P patients were received palonosetron 0.075 mg i.v., just before the induction of anaesthesia. Both nausea and vomiting were assessed for 24 h post operatively. "Incidence of post operative nausea and vomiting" was significantly less in the group P (0%) as compared to group O (16%) ($p<0.05$) during the time period of 0-6 hrs and for the time periods of 6-24 hrs incidence was significantly less in the group P (4%) as compared to group O (20%) ($p<0.05$). Palonosetron 0.075 mg is more effective than Ondansetron 4 mg for prevention of PONV up to 24 hrs post operatively.

Keywords: PONV, Palonosetron, Ondansetron, Laparoscopic surgery, Nausea, Vomiting

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INTRODUCTION

Postoperative nausea and vomiting (PONV) is the most common complication of surgery and anesthesia leading to adverse consequences including patient dissatisfaction, unexpected hospital admission, delayed recovery and return to work, wound dehiscence and surgical site bleeding [1-3]. The incidence of PONV can reach 80% in high-risk patients, underlining the importance of prevention and control by anaesthetists [4].

Despite significant advances in the delivery of general anesthesia, post-operative nausea and vomiting [PONV] continues to be a 'Big little problem' for surgical patients [5].

Gynecological, middle ear, laparoscopic, and ophthalmic surgery have more risk of PONV.

Laparoscopic procedures represent a highly susceptible group for PONV due to Factors like

- Increase abdominal pressure and volume (Pneumoperitoneum)
- Patient in extreme position
- Carbon dioxide insufflations which may leadshypercarbia

Anti-emetics (cholinergic-muscarinic, dopaminergic, histaminic or seratonergic) are the main stay therapy for PONV. Besides this, Dexamethasone is also considered very effective antiemetic in many situations.

The 5-hydroxytryptamine-3 (5-HT3) receptor antagonists are popular drugs for PONV prophylaxis because of their similar efficacy to Droperidol or Dexamethasone and their favorable side-effect profile [2]. Ondansetron with a half life of (3-4hrs) require frequent dosing. Palonosetron is a new, potent, selective 5-HT3 receptor antagonist with a strong receptor binding affinity and a long elimination half life and, therefore, a long duration of efficacy [6,7]. A study evaluating the efficacy of Palonosetron in preventing PONV found that a single 0.075 mg intravenous(i.v.) dose significantly decrease incidence of PONV during the first 24hr after anesthesia, in patients undergoing laparoscopic surgery [8]. It was also reported that Palonosetron is as effective as ondansetron in preventing chemotherapy-induced nausea and vomiting following highly emetogenic chemotherapy [9], although no study has evaluated the relative efficacy of palonosetron and ondansetron in preventing PONV.

The present randomized, double-blind study was designed to evaluate the efficacy of palonosetron compared with ondansetron for preventing PONV in patients undergoing laparoscopic surgery.

SUBJECTS AND METHODS

After obtaining the institutional ethical committee approval and written informed patient consent, randomly selected 100 patients of either sex from the age group of 18-60

years of ASA risk I and II undergoing general anesthesia for various laparoscopic surgical procedure were included for study.

Exclusion Criteria

- History of motion sickness
- Past history of PONV
- Pregnant and menstruating women
- Received any anesthetic in last 24 hrs
- Body mass index >35

Routine laboratory investigations like hemoglobin, random blood sugar, renal function test, serum bilirubin, X-rays and ECG were recorded. Patients were not given any solid or liquid food after 10 pm on the previous night before operation. No pre-medication was given in the ward.

The patients were divided into 2 GROUPS, classified as

Group	**Drug received**
G (O)	4mg i.v.
G (P)	0.075mg i.v.

The drug was administered 5 min after induction in all the groups.

After taking the patient on the OT table, IV line was established, monitors were applied and baseline pulse and BP were recorded.

Pre medication

inj. Glycopyrrolate (0.004 mg/kg) i.v.
inj. Midazolam (0.02 mg/kg) i.v
inj. Fentanyl (2 µg/kg). i.v.

Patients were pre-oxygenated with 100% O2. General anesthesia was administered with inj.Thiopentone Sodium 5-6mg/kg IV and inj.Scoline 2mg/kg IV and intubated with appropriate size oral portex cuffed endotracheal tube. Bilateral air entry was checked and tube was fixed. Nasogastric tube was inserted and stomach content suctioned.

In group (O) inj. Ondansetron 4 mg i.v. and in group (P) inj. Palonosetron 0.075 mg in 10 ml 0.9% saline was given.

Anesthesia was maintained with O2 + N2O + Isoflurane + Vecuronium Bromide (0.08mg/kg iv). Intra-operative pulse, BP, SpO2, ECG and ETCO2 were monitored and documented at the time of induction then every 15 mins up to 1 hour then every 30 mins till

the end of surgery. Inj. Diclofenac Sodium (2mg/kg) IV was given as an analgesic at the end of surgery. After completion of surgery, neuromuscular blockade was reversed with inj. Glycopyrrolate (0.008mg/kg) and inj. Neostigmine (0.05mg/kg) IV. Extubation was done after adequate oropharyngeal and endotracheal suctioning.

Patients were monitored for emetic episodes, severity of nausea, requirement of rescue antiemetic and vital signs for immediate, 1 hour, 2-6 hour, 6-12 hour and 12-24 hour post operative period that began when the patient responded to a vocal command after extubation. Metoclopramide 10mg/kg IV was given as a "rescue" antiemetic for vomiting or persistent nausea, if 2 or more episodes occurred within 24 hrs. Adverse events (rash, headache and diarrhea) within 24 hrs of surgery were also assessed and noted and treated.

No distinction was made between vomiting and retching for data collection. **Vomiting** was defined as expulsion of stomach contents through the mouth. **Retching** was defined as an involuntary attempt to vomit that did not produce stomach contents. An **emetic episode** was defined as a vomiting or retching events or combination of these events that occurred in rapid succession. **Complete response** was defined as no PONV and no administration of rescue antiemetic medication during the first 24 hours of anesthesia.

Nausea and vomiting were evaluated as:-

Score		**Events**
0	-	Complete response
1	-	Nausea
2	-	Nausea and vomiting

The efficacy of the study medication was assessed in terms of percentage of patients having complete response and mean PONV score.

Statistical analysis was performed with One-way analysis of variance (ANOVA) and Student's t-test for continuous variables with the use of EPI INFO software. Discrete variables, such as frequency of PONV and incidence of adverse effects were compared with Chi-Square test. A 'p' value <0.05 was considered significant.

RESULTS

Comparative study between use of ondansetron and palonosetron to prevent post operative nausea and vomiting was done among 100 patients of either sex undergoing different type of laparoscopic surgeries under general anesthesia. The following observation and results were recorded.

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Table 1: Study participant demographic data

Demography parameter	Group (O)	Group (P)	P-Value
Age (M ± SD)	36.62±14.35	36.67±12.05	0.95
Sex F/M	35/15	30/20	0.40
Weight (M±SD)	53.22±12.63	52.90±13.33	0.90
Duration of anesthesia (M±SD)	79.66±12.00	81.66±23.60	0.60

Table 2: Type of surgery

Type of surgery	Group(O) No. of patients	Group(P) No.of patients
Appendicectomy	14	17
Diagnostic laproscopy	4	11
cholecystectomy	30	21
Hernioplasty	2	1

Table 3: Hemodynamics

Time	Group (P) (M±SD)	Group(O) (M±SD)	P value
Immediate			
Pulse	80.58±5.54	77.98±5.07	0.23
SBP	125.92±5.48	125.36±6.92	0.65
DBP	79.08±4.21	78.08±3.18	0.18
1 hr.			
Pulse	80.88±4.37	80.06±4.61	0.36
SBP	124.84±6.49	124.90±8.21	0.96
DBP	78.24±3.19	78.76±4.46	0.50
2-6 hrs.			
Pulse	80.88±4.37	80.06±4.61	0.36
SBP	125.92±5.48	125.92±5.48	1.00
DBP	79.08±4.24	78.08±3.18	0.18
6-12 hrs.			
Pulse	80.48±4.59	77.98±5.07	0.45
SBP	125.92±5.48	125.92±5.48	1.00
DBP	79.12±4.20	79.08±4.24	0.96
12-24 hrs.			
Pulse	82.48±4.59	78.98±5.07	0.34
SBP	125.86±4.56	125.82±5.45	0.97
DBP	78.36±3.12	79.08±4.24	0.33

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Table 4: Incidence of Nausea and Vomiting At Different Time Periods

Time	Group (P)	Group (O)	P value
Immediate			
Complete response	47 (94%)	42 (84%)	0.03
Nausea	3 (4%)	7 (12%)	0.02
Vomiting	0 (0%)	1 (2%)	0.8
Total(MEAN ±SD)	0.08±0.34	0.22±0.58	0.004
1 hr			
Complete response	47 (94%)	42 (84%)	0.03
Nausea	3 (4%)	7 (12%)	0.02
Vomiting	0 (0%)	1 (2%)	0.8
Total(MEAN±SD)	0.08±0.34	0.22±0.58	0.004
2-6 hrs			
Complete response	47 (94%)	42 (84%)	0.03
Nausea	3 (4%)	7 (12%)	0.02
Vomiting	0 (0%)	1 (2%)	0.8
Total(MEAN±SD)	0.08±0.34	0.22±0.58	0.004
6-12hrs			
Complete response	46 (94%)	40 (84%)	0.03
Nausea	3 (4%)	8 (12%)	0.02
Vomiting	1 (0%)	2 (2%)	0.8
Total(MEAN±SD)	0.08±0.34	0.22±0.58	0.004
12-24hrs			
Complete response	46 (94%)	40 (84%)	0.03
Nausea	3 (4%)	8 (12%)	0.02
Vomiting	1 (0%)	2 (2%)	0.8
Total (MEAN±SD)	0.08±0.34	0.22±0.58	0.004

Table 5: Rescue Antiemetic

Rescue antiemetic	Group (O) No. of patients	Group (P) No. of patients	P-Value
Immediate	1	0	0.5
1st hr	1	0	0.3
2-6 hrs	1	0	0.3
6-12 hrs	0	1	0.24
12-24 hrs	2	1	0.8

In our study, both the groups were comparable with regards to age, sex, weight, duration of anesthesia and type of surgery (P>0.05)(table 1)(table 2).

The hemodynamic parameters pulse, SBP, DBP were not significantly different at various time interval and statistically comparable in both groups (p>0.05) (table 3).

Incidence of "**complete response**" in group (O) and group (P) in the time periods of immediate, 1 hrs, 2-6 hrs, 6-12 hrs and 12-24 hrs are 84% and 94%, 84% and 94%, 84% and 94%, 80% and 94%, 80% and 94% (with $p < 0.05$) respectively which suggest incidence of complete response was statistically higher in group (P) as compared to group (O).

"Incidence of post operative nausea and vomiting" was significantly less in the group (P)(0%) as compared to group (O) (16%)($p<0.05$) during the time periods of immediate, 1 hr and 2-6 hrs. Incidence of post operative nausea and vomiting was significantly less in the group P (4%) as compared to group 0 (20%)($p<0.05$) in the time periods of 6-12 hrs and 12-24 hrs. So in our study incidence of nausea and vomiting is clinically and statistically less in group (P) as compares to group (O).

As per table 5, While 10% patients in group (O) require rescue anti emetic compared to 4% patient in group (P) in 0-24 hrs ($p > 0.05$).

DISCUSSION

PONV continues to be a "BIG LITTLE" [10] problem for surgical patients in spite of significant advances in delivery of general anaesthesia. PONV occurs with high frequency and is distressing to patients and potentially affect the post-operative recovery, and there by hospital stay. PONV may lead to significant morbidity from dehydration, electrolyte imbalance, and aspiration of vomiting. Surgical complication like wound dehiscence and bleeding beneath skin flaps may follow severe PONV.

The newest class of antiemetic used for the prevention and treatment of PONV are the serotonin receptor antagonists (Ondansetron, Granisetron, Dolasetron, Palonosetron). Headache and dizziness are the main adverse effects of the serotonin receptor antagonists.

We conducted a study to compare the efficacy of Ondansetron (group O) and Palonosetron (group P) during laparoscopic surgery to prevent PONV.

Ondansetron is a potent, highly selective 5-HT3 receptor antagonist. The mechanisms of action of Ondansetron are both central and peripheral. It blocks the 5-HT3 in the area postrema, nucleus tractus solitarius (NTS) and adjacent areas in the brain, which are related to nausea and vomiting. Also, it blocks 5-HT3 receptors in the mucosal vagal afferents in the gastrointestinal tract.

Palonosetron is a "second generation" 5HT3 receptor binding agent newly approved for the prevention of PONV since March 2008; it having 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 [11].

In 2011 Sukhminderjit singh, et al [12] did a prospective double blind study in which Group I received 8 mg of inj. Ondansetron IV while group II received inj. Palonosetron 0.075mg IV 5 min. They concluded that Palonosetron is better drug to prevent PONV in patients as compared to Odansetron in day care surgical patients due to prolonged duration of action and favorable side effect profile.

WA Bradshaw, et al [13] at 2002 found that frequency of PONV in patients undergoing laparoscopic foregut surgery was significantly increased [14]. Patients undergoing laparoscopic surgeries are known to have a higher incidence of PONV. The etiology of PONV following laparoscopic surgery remains unclear, but is probably associated with operative factors. These include the effect of intraperitoneal CO2 insufflated on residual stretching and irritation of the peritoneum [15]. A number of factors, including age, sex, obesity, anesthetic technique and postoperative pain are also considered to increase the incidence of PONV after general anaesthesia for elective surgery [16]. In this study, however, the treatment groups were similar with regard to patient demographics (table-1), duration of anaesthesia (table-1) and type of surgery (table-2). Therefore, the difference in the incidence of PONV among the groups can be attributed to the different antiemetic drug administered.

As per table 3, the hemodynamic parameters at various time periods did not show any statistical or clinical difference in both the groups.

While analyzing results of our study, as per (table 4), the incidence of "complete response" was statistically higher in group (P) as compared to group (O).

In 2010 Dhurjoti Prosad Bhattacharjee, et al conducted a Comparative Study between Palonosetron and Granisetron to Prevent Postoperative Nausea and Vomiting after Laparoscopic Cholecystectomy. The incidence of a complete response (no PONV, no rescue medication) during 0-3 hour in the postoperative period was 86.6% with granisetron and 90% with Palonosetron, the incidence during 3-24 hour postoperatively was 83.3% with granisetron and 90% with Palonosetron**.** So our results are comparable with above study.

"Incidence of post operative nausea and vomiting" was significantly less in the group P (0%) as compared to group O (16%) ($p<0.05$), during the time periods: immediate, 1 hr and 2-6 hrs. Incidence of post-operative nausea and vomiting was significantly less in the group P (4%) as compared to group 0 (20%) ($p<0.05$) in the time periods: 6-12 hrs and 12-24 hrs. So in our study incidence of nausea and vomiting was clinically and statistically less in group (P) as compared to group (O).

In 2011 SK PARK, et al conducted a randomized, double-blind study to evaluate the relative efficacy of Palonosetron and Ondansetron in preventing postoperative nausea and vomiting (PONV) in patients undergoing gynecological laparoscopic surgery [17]. The incidence of PONV was significantly lower in the Palonosetron group compared with the Ondansetron group (42.2% and 66.7% respectively). So our results are comparable with above study.

As per table 5, no patient in group (P) required rescue anti-emetic as compared to 6% patients in group (O) in immediate, 1 hr, and 2-6 hrs time periods ($p > 0.05$). While 10% patients in group (O) required rescue anti emetic compared to 4% patient in group (P) in 6-12 hrs and 12-24 hrs ($p > 0.05$).

So in our study there was no statistical significant difference in 2 groups for requirement of rescue anti-emetics.

In 2011 Sukhminderjit singh Bajwa,et al [12] did a prospective double blind study. Group I received 8 mg of inj. Ondansetron iv while group II received inj. Palonosetron 0.075mg iv. The mean rescue dose of anti emetic is significantly higher in group I (10.6 mg) as compare to group II (6.4mg) ($P = 0.036$). So our results were comparable.

In our study Palonosetron was more effective than Ondansetron for prophylaxis against post operative nausea in the first 6 hrs. Palonosetron was more effective than Ondansetron in decreasing the incidence of vomiting over the 24 hrs. No. of Patients requiring the use of rescue anti emetics were significantly less in the group (P) as compared to group (O) within the 24 hrs. Ondanosetron was not as much as effective for prevention of PONV up to 24 hrs.

CONCLUSION

The conclusion of our study:

- Palonosetron is highly effective for prophylaxis of PONV.
- Its optimal and cost effective dose is 0.075 mg.
- Due to its longer duration of action, single dose of Palonosetron is highly effective for prevention of PONV up to 24 hrs post operatively.
- It has minimal side effects and no effect on hemodynamic parameters.
- Palonosetron 0.075 mg is more effective than Ondansetron 4 mg for prevention of PONV up to 24 hrs post operatively.

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