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Comparative Study of Palonosetron and Ondansetron for the Prevention of Post Operative Nausea and Vomiting In Patients Undergoing Laproscopic Surgeries

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Abstract:*Nausea and Vomiting are the most common and unpleasant side effects associated with the use of anaesthetic techniques for surgical procedure. The incidence of Postoperative nausea and vomiting is 20% - 30%. PONV results in increased patient discomfort, dissatisfaction, worry to relatives and increased cost related to the length of hospital stay.*
AIMS AND OBJECTIVES To compare the efficacy of intravenous palonosetron and intravenous ondansetron for prevention of post-operative nausea and vomiting in patients undergoing laproscopic surgeries.
MATERIALS AND METHODS:We conducted this study on sixty patients under ASA I or ASA II scheduled for elective laparoscopic procedures. There patients were randomly assigned to one of the two groups each containing 30 patients, using computer generated random allocation chart. Group P consisted of patients receiving inj. Palaonosteron 0.o75 mg and in group O patients received inj. Ondansteron 4 mg. All patients were induced with inj.Propofol 2 mg/kg. Hemodynamic variables were continuously monitored till the end of surgery. Post-operative nausea and vomiting were recorded at 0, 1 ,6,12, 24 hrs after the surgery.RESULTS:The demographic profile was comparable. Statistically the incidence of PONV in both the groups were comparable. There was no significant difference in the effect by palonosetron versus ondansetron and both were equally effective against PONV and without any side effects. The quality of oral intake could not be assessed in either of the groups due to limitations by surgical procedure.
CONCLUSION: Palonosetron is neither inferior nor superior and is comparable to ondansetron in PONV prophylaxis in laparoscopic patients, with a stable haemodynamic profile and with no significant side effects.
Keywords: *Ondansetron, Palanosteron, PONV Prophylaxis , Laparoscopic surgeries.*

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I. Introduction

Postoperative nausea and vomiting (PONV) is a common and distressing complication of surgery under general anesthesia. Its overall incidence can rise to 80% in high-risk patients.[1] The incidence of PONV remains unacceptably high (40-75% in the first 24hrs, without active intervention) following laparoscopic proceddures.[2,3]

PONV results in increased patient discomfort, dissatisfaction and increased cost related to the length of hospital stay. Apart from patient discomfort, PONV is associated with adverse effects, such as delayed recovery and prolonged hospital stay.

Although rare, postoperative morbidities including wound dehiscence, pulmonary aspiration, bleeding, and dehydration that can occur if vomiting is prolonged.

Laparoscopic surgery involves insufflation of a gas (usually carbon dioxide) into the peritoneal cavity producing a pneumoperitoneum. This causes an increase in intra-abdominal pressure (IAP). Carbon dioxide is insufflated into the peritoneal cavity at a rate of 4–6 litre min^{-1} to a pressure of 10–20 mm Hg. The pneumoperitoneum is maintained by a constant gas flow of 200–400 ml min^{-1}. The raised intra-abdominal pressure of the pneumoperitoneum, alteration in the patient's position and effects of carbon dioxide absorption cause changes in physiology. Increased IAP may cause regurgitation of gastric contents with associated risk of pulmonary aspiration. This is particularly significant in the obese patient.

The management of nausea and vomiting has improved greatly in recent years, with the introduction 5-HT_3 receptor antagonists. The commonly used drug to prevent PONV is ondansetron. These drugs exert there there effect by binding to serotonin 5-HT_3 receptors in chemoreceptor trigger zone (CTZ) and vagal afferents in gastrointestinal tract Most clinical research with the 5-HT_3 receptor antagonists has used ondansetron, and its

antiemetic efficacy is well established in chemotherapy- induced emesis and in the treatment and prevention of PONV. However, several alternatives to ondansetron (e.g. granisetron, tropisetron, dolasetron, ramosetron) are now available.Recently, palonosetron has been reported to be effective against chemotherapy-induced nausea and vomiting [3,4] and effective in the prevention of PONV [5,6].

To date, however, there are few clinical studies comparing the prophylactic efficacies of ondansetron and palonosetron in high-risk patients with PONV. We therefore evaluated the antiemetic effectiveness of IV palonosetron, administered as a single pre-induction dose, in laparoscopic surgeries during the first 24 postoperative hours, using the prototype 5-HT_3 receptor antagonist ondansetron as comparator drug.

II. Methodology

We conducted this study on sixty patients under ASA I or ASA II scheduled for elective laparoscopic procedures. There patients were randomly assigned to one of the two groups each containing 30 patients, using computer generated random allocation chart. Group P consisted of patients receiving inj. Palaonosteron 0.o75 mg and in group O patients received inj. Ondansteron 4 mg. All patients were induced with inj.Propofol 2 mg/kg. Hemodynamic variables were continuously monitored till the end of surgery. Post-operative nausea and vomiting were recorded at 0 ,1 ,6,12,24 hrs after the surgery.
The following were thes basis of the selection of various patients.

INCLUSION CRITERIA:
- . ASA grade I or II fit patients.
- Ages between 20 and 60 years of either sex
- Haemodynamically stable patients with all routine investigations within normal limits without any other co morbidities.
- Patients who are not on any cardiac related drugs.
- Availability of informed consent.

EXCLUSION CRITERIA:
- Patients with ASA physical status III or more.
- Patients below 20 years and above 60 years of age.
- Patients posted for emergency procedures.
- Patients with major neurological, cardiac, respiratory, metabolic, renal, hepatic disease or with coagulation abnormalities.
- Patients with history of motion sickness or previous PONV.
- Patient who have taken antiemetic drugs within 24 hours before surgery.
- Patients with cardiac co-morbidities.
- Patients with known allergies to the study drugs.
- Pregnant patients

During the surgery, monitoring was done and only vitals were noted as follows:
- Continuous pulse rate monitoring
- Continuous blood pressure monitoring (S.B.P, D.B.P, Mean B.P)
- Oxygen Saturation

These parameters were monitored in following time pattern:
T0- baseline (before induction of drug)
T5- 5 minutes after induction of drug and general anaestheisa
T10 – 10 minutes after general anaesthesia
T15- 15 minutes after general anaesthesia
T30 – 30 minutes after general anaesthesia

Patients were also monitored for any changes in the vitals suggestive of side effects of the study drugs.
Post- operatively, vitals including pulse rate, non invasive blood pressure, pulse oximetery using a portable pulse oximeter were monitored again and any signs and symptoms nausea and vomiting were noted using the PONV score at 1 hour, 6 hours, 12 hours and 24 hours interval.
T1 – 1 hour post operatively
T6 – 6 hours post-operatively
T12 - 12 hours post- operatively
T 24 – 24 hours post-operatively

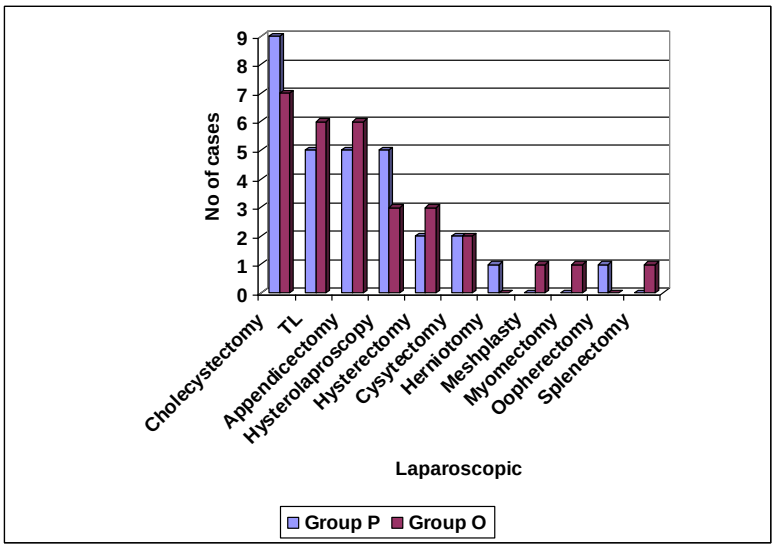
SCORE TABLE TO ASSESS POST-OPERATIVE NAUSEA AMD VOMITING IS AS FOLLOWS:

0 1 2 3

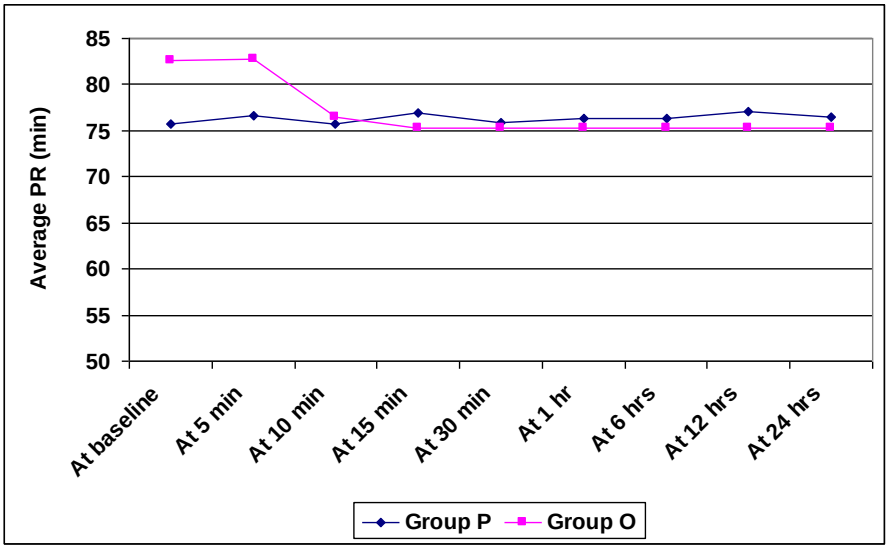
SCORE TABLE:
0- NO SYMPTOM
1- MILD NAUSEA
2- SEVERE NAUSEA BUT NO VOMITING
3- VOMITING

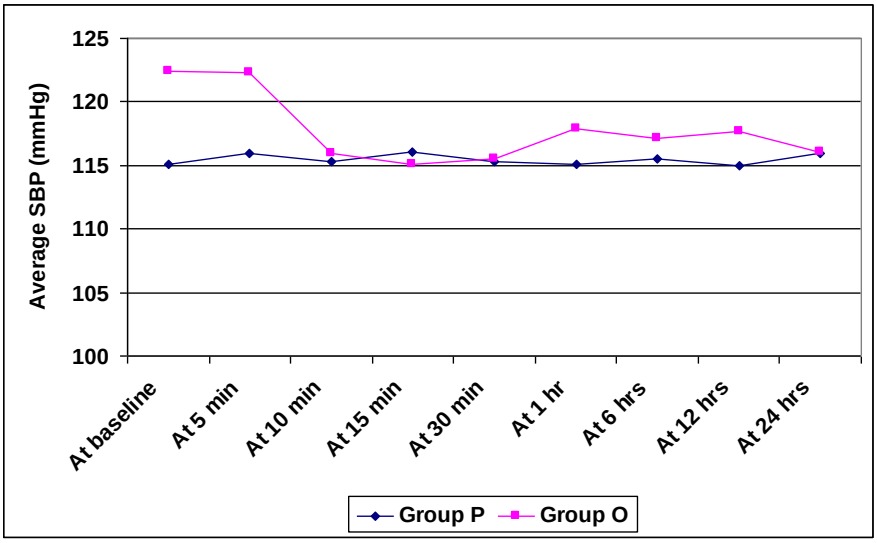
III. Results

The demographic profile was comparable. Statistically the incidence of PONV in both the groups were comparable. There was no significant difference in the effect by palonosetron versus ondansetron and both were equally effective against PONV and without any side effects. The quality of oral intake could not be assessed in either of the groups due to limitations by surgical procedure.

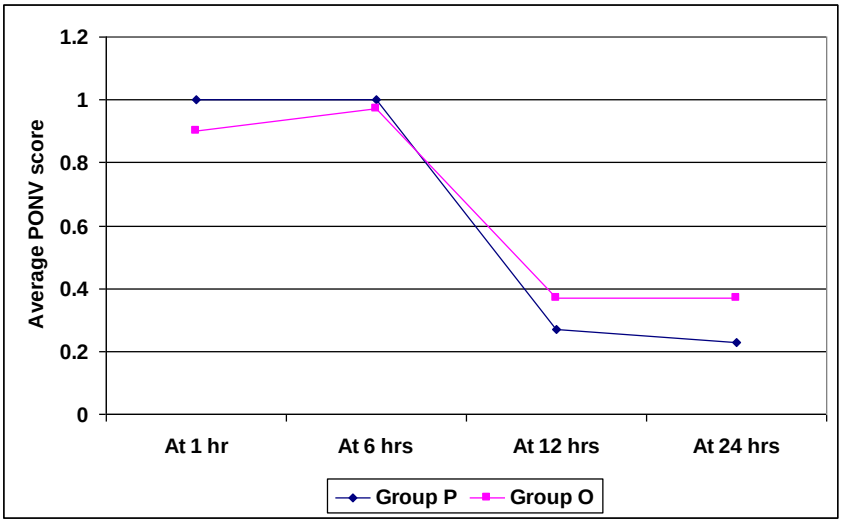


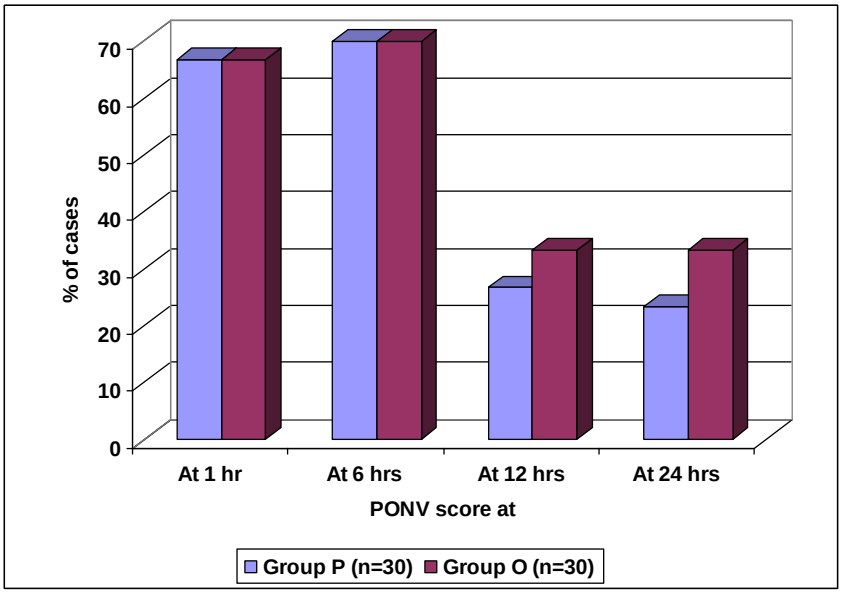
The above table shows the different types of surgeries under the two study groups. Though the type of surgery are different for the two groups, method of surgery that is laparoscopic way was the same for both groups.
The following diagrams describe the details of the vitals.





Comparison of PONV score was displayed as:





The comparison of PONV score as percentage of cases in the two groups. It was seen that the PONV score is similar at 1 hour and 6 hours in both the groups. At the intervals of 12 hours and 24 hours, group P shows more percentage of cases with a better PONV score. However this was statistically insignificant.

IV. Discussion

The management of nausea and vomiting has improved greatly in recent years, with the introduction 5-HT_3 receptor antagonists. The commonly used drug to prevent PONV is ondansetron. However, several alternatives to ondansetron (e.g. granisetron, tropisetron, dolasetron, ramosetron) are now available. Recently, palonosetron has been reported to be effective against chemotherapy-induced nausea and vomiting [3,4] and effective in the prevention of PONV.

The present study was carried out to compare the effect of ondansetron and palonosetron in prevention of PONV in patients undergoing various laparoscopic surgeries as it is known that this method increases incidence of PONV. Total 60 patients were enrolled belonging to ASA I and ASA II, between 20 to 60 years undergoing laparoscopic surgeries.

Our study showed that palonosetron (0.075 mg) is non inferior to ondansetron (4 mg) in the prevention of vomiting in patients undergoing laparoscopic surgeries. The 'p' value of PONV in PACU, PONV after 1 hours, 6 hours, 12 hours and 24 hours are 1, 1, 0.57 and 0.39 respectively. Since these values are greater than 0.05, these parameters didn't differ from both groups significantly.

These findings were found similar with the findings of the following studies:

In **2013, SooYeong MoonEt. al**, did a comparison of palonosetron with ondansetron in prevention of postoperative nausea and vomiting in patients receiving intravenous patient-controlled analgesia after gynecological laparoscopic surgery.One hundred non-smoking female patients scheduled for gynecological laparoscopic surgery were randomly assigned into the palonosetron group (n = 50) or the ondansetron group (n = 50). Palonosetron 0.075 mg was injected as a bolus in the palonosetron group. Ondansetron 8 mg was injected as a bolus and 16 mg was added to the IV-PCA in the ondansetron group. The incidences of nausea, vomiting and side effects was recorded at 2 h, 24 h, 48 h and 72 h, postoperatively.There were no significant differences between the groups in the incidence of PONV during 72 h after operation. However, the incidence of vomiting was lower in the palonosetron group than in the ondansetron group (18% vs. 4%, P = 0.025). No differences were observed in use of antiemetics and the side effects between the groups.They concluded that the effects of palonosetron and ondansetron in preventing PONV were similar in high-risk patients undergoing gynecological laparoscopic surgery and receiving opioid-based IV-PCA.

In **2013, Laha B, Hazra A** and others did an evaluation of antiemetic effect of intravenous palonosetron versus intravenous ondansetron in laparoscopic cholecystectomy in a randomized controlled trial.A single pre-induction IV doses of palonosetron (75mcg) or ondansetron (4mg) were administered to adult patients of either sex undergoing elective laparoscopic cholecystectomy..There was no statistically significant difference between the groups in primary outcome. Similarly, the frequencies of nausea, retching and vomiting episodes, when considered individually, did not show significant difference. Nausea score was comparable at all time points. With palonosetron, 14 subjects (28.6%) required rescue medication while 13 (26.5%) did so with ondansetron. The number of complete responders was 14 (28.6%) and 16 (32.7%), respectively. Adverse events were few and mild. QT_cprolongation was not encountered. Thus, palonosetron was found comparable to ondansetron for PONV prophylaxis in elective laparoscopic cholecystectomy when administered as single pre-induction dose.

However some studies did show palonosetron to be more effective than ondansetron.

In **2011, Park and Cho**did a randomized, double-blind trial of palonosetronand compared it with ondansetron in preventing postoperative nausea and vomiting after gynaecological laparoscopic surgery.The occurrence of nausea and vomiting and the severity of nausea according to a visual analogue scale were monitored immediately after the end of surgery and during the following 24 h. The incidence of PONV was significantly lower in the palonosetron group compared with the ondansetron group (42.2% vs 66.7%, respectively). There were no significant statistical differences in the visual analogue scale for nausea. In conclusion, palonosetron 0.075 mg was more effective than ondansetron 8 mg in preventing PONV.

Dr. Neelam Singh, Dr. B.K. Raw and others,in **2016**, studied the effect of palonosetronvsondansetron for prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Palonosetron 75 µg or ondansetron 8mg was injected as a bolus before the induction of anaesthesia in their respective groups. The incidences of PONV at 0-6hrs, 6-12hrs, 12-24 hrs, incidence of complete response, need of rescue antiemetic treatment and overall patient satisfaction were recorded postoperatively. Post- operative nausea was significantly less in palonosetron group in late post- operative period and the need for rescue antiemetics was also less (22.22% vs 4.44%, p-value 0.0266). Other parameters such as early PONV, overall patient satisfaction, and adverse effect profile were comparable between both the groups. Hence the conclusion was drawn that palonosetron is more effective than ondansetron

Later a meta- analysis of various studies of palanosteron and ondansetron was carried out to clear out the controversy related to the comparison of the two drugs.

In **2017, Qili Liu, Chnegmao** and others studied the effects of palonosetron and ondansetron on prevention of post-operative nausea vomiting after laparoscopic surgeries.They searched for randomized controlled clinical trials in PubMed, Embase, and The Cochrane Library. Nine studies were enrolled in this meta-analysis and showed no statistically significant difference between palonosetron and ondansetron in the prevention of PONV in the first 24 hours after surgery (relative risk [RR], 0.62; 95% confidence interval [CI], 0.35–1.10). Palonosetron more effectively prevented vomiting at various time intervals during the first 24 hours postoperatively than did ondansetron: 0–2 hours (RR, 0.45; 95% CI, 0.26–0.78), 2–6 hours (RR, 0.74; 95% CI, 0.39–1.40), and 6–24 hours (RR, 1.20; 95% CI, 0.55–2.64). No significant differences in side effects were found between palonosetron and ondansetron (RR, 0.67; 95% CI, 0.40–1.14).

This meta-analysis demonstrated that palonosetron is not more efficacious than ondansetron in the prevention of early PONV. However,they concluded that palonosetron was more efficacious than ondansetron in the prevention of vomiting after laparoscopic surgery.

V. Limitations Of Study

The limitations of the study were:

1. The placebo control group was not included as a study group because it is well known that palonosetron and ondansetron are effective drugs for PONV prophylaxis.
2. Another limitation is the short follow-up time of only 24 hours.
3. Quality of oral intake could not be analyzed as the surgeries were abdominal and patients needed to be nil by mouth for a longer time till there was evidence of adequate intestinal motility post- operatively.

VI. Conclusion

Patients in two groups were comparable with regards to age, gender, type of surgery and ASA physical status. The study shows that there is no significant incidence of post- operative nausea and vomiting in the two study groups.

To conclude,

- Palonosteron is comparable to ondansetron in preventing nausea and vomiting
- Stable haemodynamic profile
- No significant complications
- Both the drugs may be hence useful in day care surgical procedures due to absence of side effects and patient satisfaction.

Thus, use of palonosetron and ondansetron could be effectively done in not only laparascopic surgeries but also other surgeries requiring general anaesthesia.

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