COMPARISON OF THE EFFICACY OF INTRAVENOUS PALONOSETRON AND ONDANSETRON FOR THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY- A RANDOMISED DOUBLE-BLIND CONTROLLED STUDY

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ABSTRACT

BACKGROUND
Postoperative nausea and vomiting is the most common distressing symptom after surgery. Women undergoing laparoscopic surgeries are particularly at risk. This study compares the antiemetic efficacy of ondansetron and palonosetron in females undergoing laparoscopic cholecystectomy.

MATERIALS AND METHODS
A total of 80 subjects between 18-65 years were randomly allocated into two groups of 40 each, Group O and Group P. Patients in Group O received injection ondansetron 4 mg intravenously and those in Group P received injection palonosetron 0.075 mg intravenously just prior to induction of anaesthesia. The incidence of postoperative nausea and vomiting (PONV), rescue antiemetics and any side effects were recorded in the first 24 hours. At the end of 24 hours, patient satisfaction was assessed with a 5-point scale.

RESULTS
The incidence of PONV requirement of rescue antiemetics and patient satisfaction score were comparable in both groups. There was no significant difference in side effects seen between the two groups.

CONCLUSION
The effects of palonosetron in preventing PONV was comparable to that of ondansetron after laparoscopic surgery.

KEYWORDS
PONV, Ondansetron, Palonosetron, Laparoscopic Cholecystectomy.

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BACKGROUND
Postoperative Nausea and Vomiting (PONV) is the most common unpleasant side effects of anaesthesia and surgery. The incidence of PONV increases with definite risk factors including female gender, nonsmokers, motion sickness, type and duration of surgery and use of perioperative opioids. In laparoscopic surgeries, the incidence of PONV is as high as 46-72% and this may be due to stimulation of mechanoreceptors in the gut by pneumoperitoneum. Women undergoing laparoscopic surgeries are particularly at risk. PONV is frequently complained by patients as the most distressing concern in the postoperative period, sometimes even exceeding the pain of surgery. The growing awareness to improve patient satisfaction has prompted to strive for a postoperative period, free of nausea and vomiting.

There have been many studies on methods and drugs to prevent PONV. Selective 5-Hydroxytryptamine (5-HT3) receptor antagonists are being commonly used because they are more effective in PONV prevention and treatment than other antiemetics and have fewer side effects. Ondansetron is an example of a widely used selective 5-HT3 receptor antagonist. Palonosetron is a recently introduced 5-HT3 receptor antagonist and has a receptor binding affinity higher than other 5-HT3 receptor antagonists. It has been shown that palonosetron apart from binding to the 5-HT3 receptors, it also triggers functional effects on the receptors. Both drugs are effective in preventing PONV and chemotherapy-induced nausea and vomiting. This study was an effort to compare the antiemetic efficacy of ondansetron and palonosetron in females undergoing laparoscopic cholecystectomy.
MATERIALS AND METHODS
This randomised double-blind controlled study was conducted after Institutional Research and Ethics Committee approval and written informed consent in 80 female patients of ASA physical status grade 1 and 2 aged between 18 and 65 years undergoing laparoscopic cholecystectomy under general anaesthesia. Exclusion criteria were patient’s refusal, patients on antiemetics, steroid medications and drugs known to cause emesis currently or in the immediate past, pregnant and nursing mothers and those with known hypersensitivity to the study drugs.

On the day of surgery, patients were randomised to group ondansetron (Group O) or group palonosetron (Group P) using a computer generated random number table. Patient allocation was concealed in sealed envelope. Study drugs were prepared by the anaesthesia resident not involved in the study in unlabelled syringes. 40 patients were allocated to each group. After overnight fasting, patients received Inj. Midazolam 1 mg, Inj. Morphine 0.1 mg/kg and Inj. Glycopyrrolate 0.2 mg intravenously as premedication. On the operation table, routine monitoring (ECG, pulse oximetry, NIBP, EtCO₂) were started and baseline values were noted. Patients in group O received injection ondansetron 4 mg intravenously and those in group P received injection palonosetron 0.075 mg intravenously just prior to induction. Anaesthesia was induced with Inj. Thiopentone sodium 5 mg/kg IV and Inj. Succinylcholine 2 mg/kg IV. Endotracheal intubation was done with appropriate-sized endotracheal tube. Anaesthesia was maintained with oxygen, nitrous oxide, isoflurane and vecuronium. EtCO₂ was maintained between 30-40 mmHg and intraabdominal pressure between 12-14 mmHg. At the end of procedure, patients were adequately reversed with intravenous glycopyrrolate and neostigmine and subsequently extubated after throat suction. All patients were given injection paracetamol 1 g intravenous infusion and port site infiltration with injection bupivacaine 0.25% for postoperative analgesia. All episodes of PONV were recorded for 24 hours. The rescue antiemetic prescribed was metoclopramide 10 mg intravenously. Need of rescue antiemetics, timing of first antiemetic and any side effects were recorded. At the end of 24 hours, patient satisfaction was assessed with 5-point scale as 5-very satisfied; 4-satisfied; 3-neither satisfied nor dissatisfied; 2-dissatisfied; 1-very dissatisfied.

The primary outcome in the study was the occurrence of postoperative nausea and vomiting. Chi-square test was used to compare the outcome variable between the two groups to determine the statistical significance. Patient satisfaction score was analysed using ‘t’ test. Data analysis was performed using the software SPSS 14 and Microsoft Office Excel 2007.

RESULTS
Both groups were comparable in terms of age, body weight and duration of surgery. All patients were females (Table 1).

In the immediate 2 hours postoperative period, 77.5% on ondansetron group and 85% in palonosetron group were free of emesis. Neither of the two groups had more than one episode of vomiting. The p value in this period was 0.390, which indicated that both ondansetron and palonosetron were equally effective in the immediate postoperative period. In the 2-12 hours period postoperatively, both groups displayed similar statistics, 5% of both groups had vomiting, others were free from emesis. The p value was 1.000, which was not significant. After 12 hours, no one in the palonosetron group experienced nausea and vomiting, but 2 in the ondansetron group had vomiting. But, p value was 0.152 indicating that both the drugs were equally effective in the first postoperative day (Table 2, Figure 1).

Of the 80 patients studied, 72 patients (90%) were satisfied with the intervention for PONV. Both the groups displayed good PONV management with no significant differences.

Table 1. Demographic Data

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Group P (Mean)</th>
<th>Group O (Mean)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>55.35</td>
<td>56.58</td>
<td>0.150</td>
</tr>
<tr>
<td>Duration of surgery (hours)</td>
<td>1.29</td>
<td>1.52</td>
<td>0.396</td>
</tr>
</tbody>
</table>

Table 2. PONV Episodes

<table>
<thead>
<tr>
<th>PONV Episodes</th>
<th>0-2 Hours</th>
<th>2-12 Hours</th>
<th>12-24 Hours</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group O (n=40)</td>
<td>9</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Group P (n=40)</td>
<td>6</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>P value</td>
<td>0.390</td>
<td>1.000</td>
<td>0.152</td>
</tr>
</tbody>
</table>

Table 3. Timing of Rescue Antiemetic

<table>
<thead>
<tr>
<th>First Rescue Antiemetic</th>
<th>Group O</th>
<th>Group P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (minutes)</td>
<td>77.5</td>
<td>80</td>
</tr>
</tbody>
</table>

Figure 1. PONV Episodes
difference between the two (p value=0.060). Nobody gave dissatisfaction (scores 1and 2) as their satisfaction rating. A small number comprising 8 patients (10%) had given their opinion as neither satisfied nor dissatisfied (Table 4).

<table>
<thead>
<tr>
<th>Satisfaction Scale</th>
<th>Group O (n=40)</th>
<th>Group P (n=40)</th>
<th>Total (n=80)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>27</td>
<td>62</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Mean Value</td>
<td>3.9±0.379</td>
<td>4.15±0.533</td>
<td></td>
</tr>
</tbody>
</table>

Table 4. Satisfaction score

There was no significant difference in side effects between the two groups (Table 5).

<table>
<thead>
<tr>
<th></th>
<th>Group O</th>
<th>Group P</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>0</td>
<td>1</td>
<td>0.314</td>
</tr>
<tr>
<td>ECG changes</td>
<td>0</td>
<td>1</td>
<td>0.314</td>
</tr>
<tr>
<td>Constipation</td>
<td>1</td>
<td>0</td>
<td>0.314</td>
</tr>
<tr>
<td>Dryness of mouth</td>
<td>2</td>
<td>0</td>
<td>0.152</td>
</tr>
</tbody>
</table>

Table 5. Comparison of Side Effects of the Two Drugs

DISCUSSION

The postoperative period is associated with variable incidence of nausea and vomiting depending on the type of surgery, anaesthetic agents used (inhalation agents, opioids), smoking habits, etc. In high-risk patients, the incidence of PONV can reach 80% indicating the importance of prophylaxis and control of this distressing complications.9 Our patients were at high risk for PONV as they were females for laparoscopic surgery and received inhalational anaesthetic agents and opioids.

Palonosetron, the newer 5-HT3 receptor antagonist was first approved for the prevention of chemotherapy-induced nausea and vomiting. It has greater binding affinity and longer biological half-life (about 40 hours) than older 5-HT3 receptor antagonists. Ondansetron, the most commonly used 5-HT3 receptor antagonist has a half-life of 5-7 hours. The dose of ondansetron selected for this study was within its known effective dose range. However, the dose of palonosetron used was not firmly established and extrapolated from the doses used in earlier clinical trials. Kovar and colleagues demonstrated that palonosetron 0.075 mg was the most effective dose for the prevention of PONV after major gynaecological and laparoscopic surgeries than 0.025 mg and 0.05 mg.10

Our study suggests that the antiemetic efficacy of palonosetron was comparable to that of ondansetron for preventing PONV during the first 24 postoperative hours after laparoscopic cholecystectomy. So, we could find that despite the difference in half-lives and binding affinity to 5HT3 receptors palonosetron did not have an antiemetic effect superior to ondansetron.

These results are in agreement with Laha et al and Candiotti et al studies where they found similar antiemetic effects for ondansetron and palonosetron.11,12 The results of our study show variance with some recently published studies on palonosetron in PONV prophylaxis. Moon et al found palonosetron to be more effective than ondansetron for high-risk patients receiving fentanyl based patient-controlled analgesia after thyroidectomy in the 2-24 hours postoperatively.13 In a randomised controlled trial in daycare surgery, single preinduction IV dose of palonosetron 0.075 mg proved to be superior to ondansetron 8 mg in terms of number of subjects experiencing PONV episodes and the dose of rescue antiemetic required.14 In a trial in gynaecological laparoscopic surgery, the incidence of PONV was significantly lower with palonosetron than with ondansetron, although there were no significant difference in the visual analogue scale scores for nausea.15

Bhattacharjee et al have reported that prophylactic therapy with palonosetron was more effective than granisetron for prevention of PONV after laparoscopic cholecystectomy in the 24-48 hours postoperative period, though not in the first 24 hours.16 Bhalla J et al compared ondansetron and palonosetron for prevention of PONV in laparoscopic cholecystectomy under general anaesthesia and found that palonosetron has better antiemetic effect in the first 24 hours postoperatively and less need for rescue antiemetics.17

In our study, although, the results were not statistically significant, palonosetron group had lower incidence of vomiting in the first 24 postoperative hours. Similarly, the number of patients who needed rescue antiemetic was also lower in palonosetron group than the ondansetron group. Out of the total recruits in the study, 90% patients in both groups were satisfied with the use of 5HT3 antagonists for preventing PONV episodes.

Adverse effects with single IV dose of the study drugs were not serious and there were no significant difference in the incidence of these effects between the two groups. Compared to ondansetron, palonosetron is more expensive. Routine use of palonosetron may not be possible in all patients. So, it is better to limit its use in high-risk patients for PONV, those undergoing cancer chemotherapy and in those not responding to the conventional antiemetics.

The potential advantage of combination therapy using drugs that act on different pathways in the emetic response include improved efficacy, extended duration of antiemetic effect and the possibility of using smaller doses of individual drugs compared with monotherapy. In a previous study, a combination of granisetron 3 mg and droperidol 1.25 mg was more effective in the prevention of PONV than either antiemetic alone.18 Another study found that ondansetron 4 mg plus dexamethasone 8 mg was more effective than ondansetron monotherapy for preventing PONV in patients undergoing laparoscopic cholecystectomy.19 These results suggests that palonosetron combined with either droperidol or dexamethasone could be an effective combination for the prevention of PONV.
One limitation of our study was that equipotent doses of the two drugs were not used; instead, optimal doses were used for comparison. More research is required to determine the optimal dose of palonosetron in prevention and treatment of PONV, its interaction with other antiemetics and its safety in pregnant and nursing mothers.

CONCLUSION
A single shot intravenous injection of palonosetron 0.075 mg was comparable to Inj. Ondansetron 4 mg in preventing postoperative nausea and vomiting in the first 24 hours in female patients undergoing laparoscopic cholecystectomy. Side effects were minimal and comparable in both groups. When compared to ondansetron, the higher cost of palonosetron limits its use as a routine antiemetic drug.

REFERENCES


