Post-operative Nausea and Vomiting: Comparison of the Role of Ramosetron and Ondansetron

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INTRODUCTION

The common symptom which commonly appears after any surgical intervention is post-operative nausea and vomiting (PONV), with the high incidence of 30-40%. The etiology of this symptom can be surgical or drugs of anesthetics. Few individuals have more risk for developing the PONV, the reason for which is not known. It is believed that laparoscopic surgeries have a high incidence of PONV. Laparoscopic cholecystectomy has 53-72% chances of incidence of PONV.¹

Sometimes, PONV becomes a main cause of delay in discharge of the patient, and thus, the burden on the hospital increases. It also causes patient uneasiness, thus remains a cause of concern for the anesthesiologists. The drugs such as ondansetron and granisetron are used to control PONV. In severe cases, these drugs are used in combination with other antiemetics such as droperidol and metoclopramide.² Recently, a new drug named ramosetron has been introduced which is also a 5HT3 receptor antagonist. Some studies recommend this drug to be more potent and selective than ondansetron.¹ ³ The literature related to studies on the randomized controlled trials or case-controlled studies on the use of ramosetron is lacking.

In 1990, ondansetron was first used for controlling PONV. It is the most popular drug used for controlling nausea and vomiting post-operatively, after radiotherapy and chemotherapy. The drug can be administered orally, intramuscularly, and intravenously. The serious adverse effects of this drug are allergic reactions and ECG abnormalities such as prolonged QT interval.⁴

Both ondansetron and ramosetron are selective 5HT3 receptor antagonists. These receptors are commonly

Access this article online

www.ijss-sn.com

Month of Submission : 02-2016
Month of Peer Review : 03-2016
Month of Acceptance : 03-2016
Month of Publishing : 04-2016

DOI: 10.17354/ijss/2016/198
present in vomiting inducing sites such as nucleus tractus solitarius, area postrema, and vagal afferents. These drugs act by inhibiting the binding of serotonin to the 5HT3 receptors and thus control PONV. These drugs are not only highly selective but also show little affinity for some other receptors such as histamine, dopamine, and acetylcholine (muscarinic) receptors.\(^5\)

These drugs are metabolized in the liver by isoenzymes of cytochrome P450 and do not have any major drug interactions. Thus, these are safe to administer. The only important side effect of the drug is asymptomatic alterations in electrocardiogram, mostly elongation of PT and QTc interval.\(^6,7\)

Since the literature comparing the efficacy of ondansetron and ramosetron is lacking, so we have designed a prospective, randomized, double-blind controlled study in patients undergoing laparoscopic cholecystectomy.

**MATERIALS AND METHODS**

The 150 patients aged between 25 and 55 years admitted in Teerthanker Mahaveer Medical College for elective laparoscopic cholecystectomy were divided into two groups. Ethical approval was taken from the Institutional Committee. Patients were informed about the study, and the written consent was taken. About 150 patients were divided into two equal groups \(n = 75\) by computer-generated randomization. The control group was given ondansetron, and the experimental group was given ramosetron for preventing PONV.

In the present study, the dose of the ramosetron and ondansetron used were 0.3 mg and 4 mg, respectively. Patient was pre-mediated with lorazepam (0.5 mg) orally one night before, and the patient was advised to remain nil per orally after midnight. Injection propofol 2 mg/kg and injection fentanyl 1-2 µg/kg were used to sedate the patient. During surgery, anesthesia was maintained with nitrous oxide (66%) and sevoflurane (1-2%) in oxygen. Injection vecuronium 0.1 mg/kg was given which assisted in smooth intubation. After the completion of surgery, injection diclofenac 75 mg IM was administered and later post-operative analgesia was provided by injection tramadol 2 mg/kg IM. Injection neostigmine (0.04 mg/kg) and injection glycopyrrolate (0.01 mg/kg) were given for the reversal of muscle relaxation. Before shifting the patient to post-operative room, ondansetron (4 mg) or ramosetron (0.3 mg) was administered according to the group.

With the help of an autonomous observer who was unaware or blinded of the study was used to monitor the patient for 48 h and record any complaint of nausea, vomiting, and retching. The patients who experienced significant nausea or \(>2\) episodes of vomiting, injection metoclopramide (10 mg intravenous) was given.

Nausea is defined as a subjectively disagreeable sensation related with consciousness of the desire to vomit. Retching is defined as the irregular, rhythmic contraction of the abdominal muscles without expulsion of gastric contents. Vomiting is defined as the vigorous expulsion of gastric contents from the oral cavity.\(^8\)

Nausea was calculated with the help of visual analog scale which ranges from 0 = No nausea to 10 = Nausea as worst as can be:
- Score > 5 (Severe)
- Score = 5 (Moderate)
- Score < 5 (Mild).

Retching episodes of:
- \(>2\) (Severe)
- \(=2\) (Moderate)
- \(<2\) (Mild).

All the statistical tests were two-tailed. All the values were expressed as a mean ± standard deviation. The data were recorded on standardized case report forms and analyzed in SPSS, version 17 (SPSS Inc., USA). A \(P < 0.05\) was considered statistically significant.

**RESULT**

In the present study, 150 patients who were divided into two groups underwent elective laparoscopic cholecystectomy in duration of 1 year. The difference in the mean age, height, and weight of these patients was non-significant \((P > 0.05)\). The control and experimental groups were also comparable with respect to the duration of surgery, duration of anesthesia, and duration of \(CO_2\) insufflation (Table 1).

In the early phase (\(<24\) h) of post-operative period, 53.33% in control group and 50.66% in experimental

| Table 1: Comparison of demographic data of patients and details of surgery in two groups |
|---------------------------------|-----------------|-----------------|-----------------|-----------------|
| Characteristics                  | Control group   | Experimental group |
| Age of patient (years)           | 40.42±3.69      | 40.18±2.99      | NS              |
| Height of patient (cm)           | 160.25±2.59     | 159.99±2.71     | NS              |
| Weight of patient (kg)           | 55.18±3.63      | 54.98±3.44      | NS              |
| Duration of surgery (min)        | 60.61±2.74      | 59.27±3.01      | NS              |
| Duration of anesthesia (h)       | 68.11±3.42      | 67.82±3.33      | NS              |
| Duration of \(CO_2\) insufflation (min) | 62.68±1.73      | 61.15±2.01      | NS              |

NS: Non significant \((P>0.05)\), PONV: Post-operative nausea, vomiting
group experienced PONV and retching. However, this was statistically insignificant. Whereas in the late phase (>24 h), the percentages were 28% and 13.33% in control and experimental groups, respectively, which were statistically significant ($P < 0.05$) (Table 2 and Figure 1).

Severity ratings of nausea, vomiting, and retching observed in patients of the two groups are detailed in Tables 3 and 4; Figure 2.

**DISCUSSION**

Any surgical intervention can be followed by PONV, but it is found in more than 50% of the patients undergoing laparoscopic surgery. The most important pathway for PONV is the signals received from cerebrum, receptors of viscera, and chemoreceptor trigger zone (CTZ). Besides, this in laparoscopic surgeries, the CO$_2$ insufflation also causes peritoneal distension which irritates the neurogenic pathway resulting in PONV.

Various drugs such as anticholinergics, antiserotonins, benzamides, and dexamethasone have been used as prophylaxis or treatment of PONV. However, these drugs are associated with adverse effects such as low blood pressure, dryness in oral cavity, dizziness, and extrapyramidal symptoms. 5HT3 receptor antagonists are considered as drug of choice for PONV, and they

![Figure 1: Presence of post-operative nausea and vomiting in early and late phase in both the groups](image1)

![Figure 2: Comparison of number of episodes of vomiting in two groups](image2)

### Table 2: Comparison of the incidence of PONV and retching in two groups

<table>
<thead>
<tr>
<th></th>
<th>Early phase (&lt;24 h)</th>
<th>Late phase (&gt;24 h)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Experimental</td>
<td>Control</td>
</tr>
<tr>
<td>Present</td>
<td>40</td>
<td>38</td>
<td>21</td>
</tr>
<tr>
<td>Absent</td>
<td>35</td>
<td>37</td>
<td>54</td>
</tr>
</tbody>
</table>

$P<0.05$ - significant, PONV: Post-operative nausea, vomiting

### Table 3: Comparison of severity of nausea in two groups

<table>
<thead>
<tr>
<th>Post-operative nausea</th>
<th>Early phase (&lt;24 h)</th>
<th>Late phase (&gt;24 h)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Experimental</td>
<td>Control</td>
</tr>
<tr>
<td>Absent</td>
<td>35</td>
<td>37</td>
<td>54</td>
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<tr>
<td>Mild</td>
<td>11</td>
<td>19</td>
<td>10</td>
</tr>
<tr>
<td>Moderate</td>
<td>19</td>
<td>13</td>
<td>6</td>
</tr>
<tr>
<td>Severe</td>
<td>10</td>
<td>6</td>
<td>5</td>
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</tbody>
</table>

$P<0.05$ - significant

### Table 4: Comparison of severity of retching in two groups

<table>
<thead>
<tr>
<th>Post-operative retching</th>
<th>Early phase (&lt;24 h)</th>
<th>Late phase (&gt;24 h)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
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<td></td>
<td>Control</td>
<td>Experimental</td>
<td>Control</td>
</tr>
<tr>
<td>Absent</td>
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<td>41</td>
<td>39</td>
</tr>
<tr>
<td>Mild</td>
<td>13</td>
<td>12</td>
<td>17</td>
</tr>
<tr>
<td>Moderate</td>
<td>18</td>
<td>10</td>
<td>11</td>
</tr>
<tr>
<td>Severe</td>
<td>12</td>
<td>12</td>
<td>8</td>
</tr>
</tbody>
</table>
CONCLUSION

The present study concludes that ramosetron plays a better role in controlling PONV, both in early and late phase as compared to ondansetron in laparoscopic surgeries. The severity of symptoms was also less in patients taking ramosetron. Besides this, both the drugs cause lesser side effects.

REFERENCES

5. Rabasseda X. Ramosetron, a 5-HT3 receptor antagonist for the control of nausea and vomiting. Drugs Today (Barc) 2002;38:75-89.