Tropisetron vs ondansetron for prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy: A randomized double-blind, placebo-controlled study

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Abstract
Background: Postoperative nausea and vomiting are observed in increased frequency after laparoscopic surgery. This study was performed in order to compare the efficacy of two 5-hydroxytryptamine-3 (5-HT₃) receptor antagonists, ondansetron and tropisetron, in preventing postoperative nausea and vomiting (PONV) after laparoscopic cholecystectomy.

Methods: Using a randomized, double-blind study design, 87 ASA I and II patients scheduled for laparoscopic cholecystectomy were randomly assigned to receive 4 mg ondansetron (Group A, n = 29), 5 mg tropisetron (Group B, n = 31), or placebo (Group C, n = 27) intravenously (IV) before induction of anesthesia. The end points evaluated were frequency of nausea, nausea intensity rated on a scale from 1 (mild) to 5 (most severe), frequency of vomiting, and need for rescue antiemetics. These parameters were measured immediately after surgery (0 h), at 3 h, 6 h, and 12 h postoperatively.

Results: The frequency of nausea was significantly higher in group A (31.2%) compared to group B (14%) at 12 h postoperatively (p < 0.01). However, patients of group A had significantly lower nausea scores at 3 h postoperatively compared to group B. Postoperative vomiting occurred in 13.8% of patients in group A and 9.6% of patients in group B throughout the whole study period (p = n.s.). The need for rescue antiemetics was similar between groups A and B. Both groups were superior to placebo concerning all studied parameters.

Conclusion: Our results show that ondansetron may be more effective in controlling nausea intensity during the first 3 h after laparoscopic cholecystectomy, while tropisetron has a longer-acting activity, with a major impact on nausea frequency at 12 h postoperatively.

Key words: Laparoscopic cholecystectomy — Prophylactic antiemetics — Ondansetron — Tropisetron

Postoperative nausea and vomiting (PONV) is a common and unpleasant side effect associated with laparoscopic surgery. PONV is particularly common after laparoscopic cholecystectomy with studies reporting an incidence of up to 72% [9] in placebo treated patients. Patients with PONV may require additional time in recovery room, as well as additional nursing support and medication. Persistent nausea and vomiting are the most common reasons for hospital admission after same day procedures [3, 5].

Prophylactic administration of antiemetics has been advocated in patients undergoing laparoscopic surgery as the most effective measure for prevention of PONV. Different groups of drugs have been used with varying efficacy. 5-Hydroxytryptamine-3 (5-HT₃) receptor antagonists are a class of drugs with central antiemetic action, which are widely used for preventing PONV in high-risk patients. The present study was undertaken to compare the efficacy of two 5-HT₃ receptor antagonists with different duration of action, namely the short acting ondansetron vs the more long-acting tropisetron, in the prevention of PONV following laparoscopic cholecystectomy.

Patients and methods

After approval by the hospital Ethics Committee, 87 ASA I and II patients scheduled for elective laparoscopic cholecystectomy were re-
Table 1. Patient demographics

<table>
<thead>
<tr>
<th></th>
<th>Group A, n = 29 (ondansetron)</th>
<th>Group B, n = 31 (tropisetron)</th>
<th>Group C, n = 27 (placebo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>43.9 ± 13.6</td>
<td>47.9 ± 16.7</td>
<td>41.3 ± 13.6</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>71.5 ± 14.6</td>
<td>73.4 ± 13</td>
<td>68.5 ± 8.3</td>
</tr>
<tr>
<td>Gender (m/f)</td>
<td>6/23</td>
<td>8/23</td>
<td>7/20</td>
</tr>
<tr>
<td>ASA 1/II</td>
<td>2/1</td>
<td>19/12</td>
<td>17/10</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>49.7 ± 10.3</td>
<td>51.8 ± 7.7</td>
<td>52 ± 4.5</td>
</tr>
<tr>
<td>Duration of anesthesia (min)</td>
<td>67.4 ± 15</td>
<td>75 ± 23</td>
<td>69 ± 22</td>
</tr>
</tbody>
</table>

Values are mean ± SD

cruited in this randomized, double-blinded, placebo-controlled study. Patients who had a history of PONV, motion sickness, gastrointestinal disorders, or receipt of antiemetic within 24 h before surgery were excluded from the study. During the preoperative visit the patients were introduced to the concept of the visual analog scale (VAS) for the evaluation of nausea, ranging from 1 = mild nausea to 5 = most severe nausea.

Patients were randomly allocated to one of three groups. Randomization was performed using a computer-generated randomized list. Group A (n = 29) received ondansetron 4 mg, group B (n = 31) received tropisetron 5 mg, and group C (n = 27) received placebo (saline). These drugs were administer intravenously at anesthesia induction. The syringes containing each drug were identical and were prepared by personnel not involved in the study.

Patients were premedicated with oral diazepam 0.15 mg/kg 1 h preoperatively. Anesthesia was induced with fentanyl, 3–5 μg/kg, and propofol, 2–3 mg/kg, followed by cisatracurium, 0.1 mg/kg, to facilitate tracheal intubation. The introduction of the pneumoperitoneum was achieved with open laparoscopy according to the “Hasson technique,” utilizing a cone-shaped 10–12 mm trocar (Ethicon, Cincinnati, OH, USA). The cholecystectomy was performed according to the American variable, using, apart from the Hasson trocar, one 10 mm and two 5 mm trocars. All trocar insertion sites were infiltrated before skin incision with ropivacaine (10 mg/ml) to a total of 20 ml, which was divided proportionally according to the length of the skin incision (7 ml for the 10 mm trocars and 3 ml for the 5 mm trocars). A nasogastric tube was inserted before the induction of pneumoperitoneum and was removed immediately after surgery. Anesthesia was maintained with sevoflurane 1–2%. Muscle relaxation was maintained throughout the operation with intermittent doses of cisatracurium. The use of neuromuscular reversal agents was generally avoided. The end points evaluated were (a) frequency of postoperative nausea, (b) nausea intensity for the patients who experienced nausea, rated on a scale from 1 (mild) to 5 (most severe), (c) frequency of vomiting, and (d) need for rescue antiemetics. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit. Vomiting was defined as the forceful expulsion of gastric contents from the mouth. These parameters were measured immediately after surgery (0 h), and at 3 h, 6 h, and 12 h postoperatively by anesthesia residents blinded to which antiemetic the patient had received.

For moderate or severe nausea or an episode of vomiting, metoclopramide 10 mg IV was given as rescue antiemetic. For postoperative pain relief at first nonsteroidal antiinflammatory drugs (diclofenac) were applied as suppositories. In case of pain persistence, parenteral opioids such as dextropropoxyphen or meperidine were provided. Data are expressed as the mean ± SD. Parametric data were compared between groups by analysis of variances (ANOVA) and post-hoc testing. Statistical significance was assumed, if p < 0.05. Nonparametric data were analysed using chi-square tests between groups. Analysis was performed with the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL).

Results

Eighty-seven patients were enrolled in the study. Patients’ demographics were similar in all study groups (Table 1). Both groups A and B were superior to group C concerning all studied parameters at all time intervals.

The incidence of nausea was significantly lower in group B (16.1%) at 12 h postoperatively compared to group A (34.5%) (p < 0.01). Group A showed a lower frequency of nausea at 0 h and 3 h postoperatively compared to group B, although this difference fail to reach statistical significance. At 6 h the incidence of nausea was similar in the two groups (Fig. 1).

Nausea scores were significantly lower in group A patients at 3 h postoperatively compared to group B (1.22 ± 0.4 vs. 1.63 ± 0.52, p < 0.05). Group B showed lower nausea scores at 6 h and 12 h postoperatively, although the difference did not achieve statistical significance (p = n.s.) (Fig. 2).

Postoperative vomiting occurred in 13.8% of group A patients and 9.6% of patients in group B throughout the whole study period (p = 0.41).

The proportion of patients requiring rescue antiemetics throughout the whole study period did not differ significantly between group A and B (24.1% vs 16.1%, p = n.s.).

One patient from the ondansetron group complained of headache and one patient from the tropisetron group of drowsiness, side effects which could be attributed to the use of 5-HT3 antagonists.

Discussion

The relatively high incidence of postoperative nausea and vomiting after laparoscopic procedures [9], a great number of which are scheduled on an outpatient basis, may have a negative impact on the recovery of these patients, leading to additional need for antiemetic medication or prolonged hospitalization [3, 5, 11].

The etiopathogenetic mechanism of PONV after laparoscopic surgery is multifactorial, including the central action of carbon dioxide, the influence of the increased intraabdominal pressure, postoperative gastroparesis, etc.

At least four neurotransmitter systems are associated with the mediation of emetic response. 5-Hydroxytryptamine (5-HT3) receptors appear to play an important role in the pathogenesis of postoperative vomiting. The 5-HT3-receptor antagonists are very effective antiemetics, which lack side effects associated with other antiemetics such as sedation after the use of droperidol or the extrapyramidal effects after high-dose metoclopramide [13].