Ondansetron and droperidol in the prevention of postoperative nausea and vomiting

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We have performed a prospective, randomized, double-blind clinical study to assess the efficacy of ondansetron, droperidol, or both, in preventing postoperative emesis. We studied 242 patients undergoing biliary or gynaecological surgery under general anaesthesia. Shortly before induction of anaesthesia, patients received: saline i.v. (group 1, n=62); droperidol 2.5 mg i.v. (group 2, n=60); ondansetron 4 mg i.v. (group 3, n=57); or droperidol 2.5 mg with ondansetron 4 mg i.v. (group 4, n=63). Nausea occurred in 45%, 37%, 32% and 29% (P=0.234) and vomiting in 23%, 17%, 9% and 5% (P=0.016) of patients in groups 1, 2, 3 and 4, respectively, during the first 24 h. Groups 2 and 4 had greater sedation scores than group 1 during the first 3 h (P<0.01). We conclude that both droperidol and ondansetron showed a significant antiemetic effect, ondansetron was not significantly better than droperidol, and the combination of droperidol and ondansetron was better than droperidol but no better than ondansetron alone.

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Ondansetron, a 5-hydroxytryptamine type 3 (5-HT3) receptor antagonist and droperidol, a dopamine antagonist, have been shown to be safe and useful for the prevention and treatment of postoperative emesis.1 By acting via different receptors in the chemoreceptor trigger zone, the efficacy of both drugs could be greater if used together.

We have assessed the efficacy and adverse effects of ondansetron, droperidol, or both, in the prevention of postoperative emesis in patients undergoing intra-abdominal surgical procedures under general anaesthesia.

Methods and results

We studied prospectively 242 ASA I or II patients, aged 18–60 yr, undergoing elective gynaecological or biliary surgical procedures, either by laparotomy or laparoscopy. Patients were given midazolam 7.5 mg orally the night before and 90 min before arrival in the operating room. Before induction of anaesthesia, patients were allocated by random numbers to receive saline i.v. (group 1, control, n=62), droperidol 2.5 mg i.v. (group 2, n=60), ondansetron 4 mg i.v. (group 3, n=57) or droperidol 2.5 mg with ondansetron 4 mg i.v. (group 4, n=63). The syringes were coded and the anaesthetist and investigator were blinded to the drug administered. General anaesthesia was induced with thiopental 4–6 mg kg⁻¹, fentanyl up to 3 µg kg⁻¹ and vecuronium 0.1 mg kg⁻¹, and the trachea intubated. A gastric tube was inserted and gastric contents aspirated. Anaesthesia was maintained with isoflurane and 50% nitrous oxide in oxygen. At the end of surgery, neostigmine and atropine were given to antagonize residual neuromuscular block, the trachea was extubated and the gastric tube withdrawn. Postoperative analgesia was achieved with ketorolac 30 mg i.v. qid, and morphine 2 mg i.v. on request. No other sedative drugs were given during the first postoperative day.

Nausea and vomiting were assessed at 1, 2, 3, 6, 9, 12 and 24 h in the postoperative period, in addition to sedation (0=awake; 1=drowsy; 2=asleep, responds to verbal commands; 3=asleep, responds to physical stimulus). Pain was assessed at 6, 12 and 24 h using a 10-cm visual analogue scale, and analgesic requirements were consigned.

Statistical analysis included chi-square and Kruskal–Wallis tests to compare nausea and vomiting, and ANOVA, Kruskal–Wallis and chi-square tests for comparison of patient data, analgesic requirements, pain and sedation level.

There were no differences between groups in patient data, type of surgery or previous history of sickness. During the first 24 h, the incidence of nausea was 18%, 29% and 36% less frequent in groups 2, 3 and 4, respectively.
Table 1 Patient characteristics and morphine requirements (mean (sd or range) or number) and incidence of postoperative nausea and vomiting (%) (95% confidence intervals) during the first 24 h after operation

<table>
<thead>
<tr>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>39 (18–60)</td>
<td>38 (18–60)</td>
<td>38 (19–60)</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>161 (7)</td>
<td>162 (6)</td>
<td>161 (7)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67 (11)</td>
<td>63 (10)</td>
<td>64 (10)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>14/48</td>
<td>11/49</td>
<td>13/44</td>
</tr>
<tr>
<td>Morphine (mg)</td>
<td>3.5 (2.7)</td>
<td>2.8 (2.5)</td>
<td>3.2 (2.5)</td>
</tr>
<tr>
<td>Nausea 0–6 h</td>
<td>42 (30–54)</td>
<td>32 (20–44)</td>
<td>26 (15–37)</td>
</tr>
<tr>
<td>Nausea 0–24 h</td>
<td>45 (33–57)</td>
<td>37 (25–49)</td>
<td>32 (29–44)</td>
</tr>
<tr>
<td>Vomiting 0–6 h</td>
<td>18 (8–28)</td>
<td>15 (6–24)</td>
<td>7 (0–14)</td>
</tr>
<tr>
<td>Vomiting 0–24 h</td>
<td>23 (13–34)</td>
<td>17 (8–27)</td>
<td>9 (2–17)</td>
</tr>
</tbody>
</table>

compared with group 1, but this was not statistically significant (Table 1). The incidence of vomiting in patients receiving droperidol, ondansetron and ondansetron with droperidol in the first 24 h was reduced by 26%, 61% and 78%, respectively, compared with group 1 ($P = 0.016$). At 24 h, both droperidol and ondansetron showed a significant antiemetic effect compared with controls, ondansetron was not significantly better than droperidol, and the combination of droperidol and ondansetron was significantly better than droperidol but no better than ondansetron alone.

Compared with patients in group 1, mean sedation scores were significantly higher during the first 3 h after operation in those receiving droperidol and droperidol with ondansetron. There was no difference between groups in pain scores or morphine requirements during the first postoperative day. There were no cases of profound sedation, or pulmonary or cardiovascular complications.

**Comment**

Because antiemetic drugs have several mechanisms of action, it seems reasonable to combine drugs to obtain a greater antiemetic action. In chemotherapy-induced emesis, in which the emetic stimulus is unique and well known, antiemetic drug combinations have been shown to be highly effective in the treatment of vomiting. \(^2\) In contrast, emesis after surgery is triggered by different stimuli, not all well defined, \(^1\) and few studies have shown benefits of combining two or more antiemetic drugs in this setting. Michaloudis and colleagues showed that sub-therapeutic doses of droperidol, metoclopramide and hyoscine were more effective than droperidol 1.25 mg alone for the prevention of emesis after gynaecological laparoscopy. \(^3\) In an earlier study by Pandit and colleagues, droperidol 10 and 20 µg kg\(^{-1}\) were as effective as droperidol 10 µg kg\(^{-1}\) with metoclopramide 5 mg in preventing emesis in gynaecological outpatients. \(^4\) McKenzie and colleagues found that ondansetron with dexamethasone, given before major gynaecological surgery, was better than ondansetron alone in preventing emesis, \(^5\) and later that droperidol–ondansetron was better than droperidol alone in reducing the incidence of emetic episodes.

Our data confirmed the additive effect of droperidol and ondansetron compared with droperidol but not with ondansetron alone. Adding droperidol to ondansetron did not increase its effectiveness but increased drowsiness significantly. Our data are consistent with those of Belo and Koutsoukos who found no differences between the combination of ondansetron 4 mg and droperidol 1.25 mg and each drug alone in 80 women undergoing gynaecological surgery. \(^6\) However, our data contrast with those of Pueyo and colleagues, who studied 100 patients subjected to abdominal surgery and found that the combination of ondansetron 4 mg and droperidol 2.5 mg was superior to each antiemetic alone and to a control group. \(^7\) Despite a similar antiemetic regimen in our study and that of Pueyo and colleagues there were some differences in study design. Pueyo and colleagues used two doses of the antiemetic, given 12 h apart, and higher doses of morphine were administered. This may explain the higher incidence of emesis in the control group. This higher incidence makes any difference between groups easier to demonstrate. Although the sample size in our study was larger than that of Pueyo and colleagues, a type II error cannot be excluded, particularly because of the low incidence of vomiting in our study.

**References**