Prevention of Postoperative Nausea and Vomiting With Antiemetics in Patients Undergoing Middle Ear Surgery

Comparison of a Small Dose of Propofol With Droperidol or Metoclopramide

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Objective: To compare the efficacy and safety of a small dose of propofol with other commonly used antiemetics, droperidol and metoclopramide, for the prevention of postoperative nausea and vomiting in patients undergoing middle ear surgery.

Design: Prospective, randomized, double-blind study.

Setting: University-affiliated teaching hospital.

Patients: Ninety patients (48 females, 42 males) scheduled for middle ear surgery.

Intervention: Patients received propofol, 0.5 mg/kg, droperidol, 20 µg/kg, or metoclopramide hydrochloride, 0.2 mg/kg, intravenously at the end of the surgical procedure. A standardized general anesthetic technique was employed throughout the surgical procedure.

Main Outcome Measure: Emetic episodes and safety assessment were performed during 2 periods—0 to 3 hours in the postanesthetic care unit and 3 to 24 hours in the ward—after receiving anesthesia.

Results: The incidence of patients who were emesis free during the 0- to 3-hour period after receiving anesthesia was 93% for those who received propofol, 73% for those who received droperidol, and 70% for those who received metoclopramide, respectively; the respective corresponding incidence during the 3- to 24-hour period after receiving anesthesia was 90%, 67%, and 60% (P < .05, overall Fisher exact probability test). No clinically adverse events were observed in any of the groups.

Conclusion: A small dose of propofol is a better antiemetic than droperidol or metoclopramide for the prevention of postoperative nausea and vomiting after middle ear surgery.


POSTOPERATIVE nausea and vomiting after (PONV) surgery are distressing and there are frequent adverse events after receiving general anesthesia during surgery,1 with a high incidence in patients undergoing middle ear surgery.2,3 Most of the antiemetics used—antihistamines (eg, hydroxyzine), butyrophenones (eg, droperidol), and dopamine receptor antagonists (eg, metoclopramide)—prevent PONV, but have undesirable adverse effects, such as excessive sedation, hypotension, dry mouth, dysphoria, restlessness, and extrapyramidal symptoms.1 The selective antagonists of serotonin-receptors (eg, ondansetron or granisetron) are effective for the prevention of PONV.4,5 However, several investigators6,7 have criticized serotonin-receptor antagonists because of their high cost. Propofol given at a small dose possesses direct antiemetic properties.8 A recent report by Honkavaara and Saarivaa9 has compared the efficacy of subhypnotic doses of thiopental sodium (1.0 mg/kg) and propofol (0.5 mg/kg) for the prevention of PONV after middle ear surgery, and also has demonstrated that propofol provides prophylaxis against emesis. However, to our knowledge, there have been no studies comparing the efficacy of propofol administration with the commonly used and well-established antiemetics droperidol and metoclopramide hydrochloride in the prevention of PONV after middle ear surgery. We conducted a prospective, randomized, double-blind study to evaluate the efficacy and safety of a small dose of propofol with droperidol or metoclopramide for preventing PONV in patients undergoing middle ear surgery.

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PATIENTS AND METHODS

Approval of our institutional review board and written informed consent from patients were obtained. Ninety patients (48 females, 42 males) with American Society of Anesthesiologists physical status I (ie, no organic, physiological, biochemical, or psychiatric disturbance), aged 25 to 68 years, and scheduled for middle ear surgery (tympanoplasty or mastoidectomy) were enrolled in the study. Patients who had gastrointestinal tract diseases, those who were pregnant or menstruating, and those who had taken antiemetics within 24 hours before surgery were excluded from the study.

Premedication consisted of orally administered diazepam, 5 mg. Anesthesia was induced with intravenous (IV) administration of a combination of thiopental sodium, 5 mg/kg, and fentanyl citrate, 2 µg/kg, and vecuronium bromide, 0.2 mg/kg, was used to facilitate tracheal intubation. After tracheal intubation, anesthesia was maintained with 1.0% to 3.0% (inspired concentration) of sevoflurane and 66% of nitrous oxide (which was replaced by air before closure of the middle ear cavity) in oxygen. Additional analgesia during surgical procedure was achieved with fentanyl citrate, 50 µg IV. Ventilation was mechanically controlled and was adjusted to keep an end-tidal PCO₂ at 35 to 40 mm Hg throughout the surgical procedure as measured by an anesthetic–respiratory gas analyzer (Ultima; Datex-Omeda Division, Instrumentarium Corp, Helsinki, Finland). Muscle relaxation was maintained with vecuronium as required. At the end of surgery, in a randomized, double-blind manner, patients IV received propofol, 0.5 mg/kg, droperidol, 20 µg/kg, or metoclopramide hydrochloride, 0.2 mg/kg. For reversal of muscle relaxation, a combination of atropine sulfate, 0.02 mg/kg, and neostigmine methylsulfate, 0.04 mg/kg, was administered IV, and then the trachea was extubated when the patient was awake. No patient had a nasogastric or an orogastric tube placed during surgery. Rectal temperature was monitored and maintained at 37°C±1°C (mean±SD) using a warming pad. Postoperatively, patients received rectally indomethacin sodium, 30 mg, when they reported pain. The use of oral narcotic analgesics was not permitted in any of the 3 groups.

All episodes of PONV (nausea, retching, or vomiting) were recorded by the nursing staff without knowledge of which antiemetic the patients had received during the 2 periods, ie, within the first 24 hours after receiving anesthesia or 0 to 3 hours in the postanesthetic care unit and 3 to 24 hours in the ward. Nausea was defined as the subjectively unpleasant sensation associated with awareness of the urge to vomit; retching was defined as the labored, spasmodic, rhythmic contraction of the respiratory muscles without the expulsion of gastric contents; and vomiting was defined as the forcible expulsion of gastric contents from the mouth. These nurses asked the patients if retching or vomiting had occurred and if they felt nauseous, with only 2 possible answers (yes/no). If 2 or more episodes of PONV occurred during the first 24 hours after receiving anesthesia, another rescue antiemetic (domperidone) was given rectally. The details of any adverse effects throughout the study were recorded by the nursing staff.

Patient demographic data were analyzed by analysis of variance with Bonferroni correction for multiple comparison and χ² test. The number of patients experiencing emetic episodes and requiring rescue medication, and the incidence of adverse events were compared with Fisher exact probability test. \( P < .05 \) was considered statistically significant. All values were expressed as mean±SD or number (percentage). Based on previous studies by Honkavaara et al² and us,³ it was calculated that 30 patients per group would be required to demonstrate a 30% difference in values for PONV (which was regarded as the primary end point) at \( \alpha = .05 \) with a power \((1 - \beta) = .8\).

The reported incidence of PONV after middle ear surgery (tympanoplasty or mastoidectomy) is 62% to 80% when no prophylactic antiemetic is given.²,³ The cause of PONV after middle ear surgery remains unclear, but probably is multifactorial.¹ A number of factors, including age, sex, obesity, a history of motion sickness, and/or previous PONV, menstrual cycle, operative procedure, anesthetic technique, and postoperative pain, are considered to affect the incidence of PONV.¹ Surgical factors also include an increased middle ear pressure caused by nitrous oxide.¹ In this study, however, these factors were well balanced among the groups, and no pressure was generated in the middle ear from diffusion of nitrous oxide, which was replaced by air before closing the tympanic membrane. Therefore, the difference in the incidence of PONV among the groups can be attributed to the drugs studied.

Propofol possesses direct antiemetic properties,⁸ and this effect is not due to the lipid emulsion (Intralipid) in the formulation of propofol.⁹ The exact mechanism by which propofol acts as an antiemetic is unknown, but propofol is not considered to have vagolytic properties.⁸ Ham-
Propofol at a subhypnotic dose (0.5 mg/kg) given at the end of surgery provides prophylaxis against PONV.9 The same dose of propofol was used in this clinical trial. The doses of other antiemetics, droperidol and metoclopramide, were chosen from the results of several studies regarding the prevention of PONV.12,13 More conventional doses of these antiemetics, droperidol, 20 µg/kg, and metoclopramide hydrochloride, 0.2 mg/kg, have been used for the prevention of PONV12,13 and have not been associated with adverse effects, such as excessive sedation and extrapyramidal symptoms.1 In our study, therefore, droperidol, 20g/kg, or metoclopramide hydrochloride, 0.2 mg/kg, was administered by IV.

For the prevention of PONV, droperidol and metoclopramide have been used often, but there are contradictory findings in reports concerning the effectiveness of these 2 antiemetics.1 We could not find any report to compare the efficacy of a small dose of propofol with droperidol or metoclopramide for preventing PONV after middle ear surgery. Our results demonstrated that the incidence of patients experiencing an emesis-free episode during the 2 study periods—0 to 3 hours and 3 to 24 hours after receiving anesthesia—was less in patients who had received propofol therapy than in those who had re-
received either droperidol or metoclopramide therapy (P<.05). This suggests that a small dose of propofol given at the end of the surgical procedure is more effective than droperidol or metoclopramide for increasing an emesis-free episode in patients undergoing middle ear surgery.

The major deficiency in our study was the failure to include a control group receiving placebo. However, we have already shown a high incidence of PONV after middle ear surgery in patients who had received placebo. Moreover, Aspinall and Goodman have shown that there is a lack of reliable clinical information concerning placebo-controlled trials of the serotonin3-receptor antagonist ondansetron for the prevention of PONV. Therefore, the control group receiving placebo was excluded from this clinical trial.

Adverse events observed in this study were not serious, and there were no differences in the incidence of headache and dizziness among the groups. Excessive sedation and extrapyramidal symptoms were not observed in any of the groups.

In conclusion, we have shown that a small dose (0.5 mg/kg) of propofol administered IV at the completion of surgery is a better antiemetic than either droperidol, 20 µg/kg, or metoclopramide hydrochloride, 0.2 mg/kg, for preventing PONV in patients undergoing middle ear surgery. Further studies are needed to compare the efficacy of propofol at small doses with a serotonin3-receptor antagonist (eg, ondansetron or granisetron) for reducing the incidence of PONV after middle ear surgery.

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### Table 3. Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>Propofol-Treated Patients (n = 30)</th>
<th>Droperidol-Treated Patients (n = 30)</th>
<th>Metoclopramide Hydrochloride-Treated Patients (n = 30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-3 Hours After Receiving Anesthesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>2 (7)</td>
<td>3 (10)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>2 (7)</td>
<td>2 (7)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td></td>
<td>3-24 Hours After Receiving Anesthesia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>2 (7)</td>
<td>2 (7)</td>
<td>2 (7)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (3)</td>
<td>1 (3)</td>
<td>1 (3)</td>
</tr>
</tbody>
</table>

* The 2 periods are 0 to 3 hours in the postanesthetic care unit and 3 to 24 hours in the ward after receiving anesthesia. Values are expressed as the number (percentage) of patients.