Prevention of PONV with granisetron, droperidol and metoclopramide in female patients with history of motion sickness

Yoshitaka Fujii MD,
Hidenori Toyooka MD,
Hiroyoshi Tanaka MD*

Purpose: Motion sickness is one of the patient-related factors associated with postoperative nausea and vomiting (PONV). This study was undertaken to assess the efficacy of granisetron, droperidol and metoclopramide for preventing PONV in female patients with a history of motion sickness undergoing major gynaecological surgery.

Methods: In a prospective, randomized, placebo-controlled, double-blind study, 120 patients received either 1.25 mg droperidol, 10 mg metoclopramide, 40 ~g.l.,g-1 granisetron or placebo (saline) iv immediately before induction of anaesthesia. A standardized anaesthetic technique and postoperative analgesia were used in all patients. During the first 24 hr after anaesthesia, the incidence of PONV and adverse events were recorded by nursing-staff.

Results: The treatment groups were similar for patient demographics, types of surgery, anaesthetics administered and opioid given. The incidence of PONV was 70%, 50%, 57% and 23% in the placebo, droperidol, metoclopramide and granisetron groups, respectively (P < 0.05; overall χ² test). No difference in the incidence of adverse events was observed in either group.

Conclusion: Granisetron is a better prophylactic antiemetic than droperidol or metoclopramide in female patients with a history of motion sickness undergoing major gynaecological surgery.

From the Department of Anesthesiology, University of Tsukuba Institute of Clinical Medicine, Tsukuba City, Ibaraki, Japan and *the Department of Anaesthesiology, Todde Kyodo General Hospital, Toride City, Ibaraki, Japan.

Address correspondence to: Dr. Y. Fujii, Department of Anaesthesiology, University of Tsukuba Institute of Clinical Medicine, 2-1-1, Amakubo, Tsukuba City, Ibaraki 305, Japan. Phone: 0298-53-3763; Fax: 0298-53-3765.

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POSTOPERATIVE nausea and vomiting (PONV) are among the most common complications following surgery performed under general anaesthesia, with female patients being particularly susceptible. The aetiology of PONV is complex and is dependent on a variety of factors, including patient demographics, type of surgery, anaesthetic technique and postoperative care. Motion sickness is one of the patient-related factors associated with PONV. Recently, we demonstrated that granisetron, a selective 5-hydroxytryptamine type 3 (5-HT3) receptor antagonist, reduced the incidence of PONV in patients with a history of motion sickness. However, there were no direct comparative studies with other commonly used and well-established antiemetics, such as droperidol and metoclopramide, for preventing PONV in patients experienced it. This study was undertaken to assess the efficacy of granisetron, droperidol and metoclopramide for preventing PONV in a prospective randomized, placebo-controlled, double-blind comparison with placebo in female patients with a history of motion sickness undergoing major gynaecological surgery.

Methods
Approval of our institutional review board and informed consent from patients were obtained. One hundred and twenty female patients with a history of motion sickness, ASA physical status I or II, aged 23 yr to 63 yr, and scheduled for major gynaecological surgery were eligible to participate. A history of motion sickness was collected as a part of the demographic information. Patients who had gastrointestinal diseases, those who were pregnant or menstruating, or those who had taken any antiemetic medication within 24 hr of surgery were excluded from the study.

Patients were randomly assigned to one of four groups (n=30 for each group) to receive pretreatment with 1.25 mg droperidol, 10 mg metoclopramide, 40 μg kg⁻¹ granisetron or placebo (saline). These drugs were administered iv over two to five minutes before induction of anaesthesia.

As premedication, patients were given 0.5 mg atropine im 30 min before induction of anaesthesia. An epidural catheter was inserted at the L2-3 or L3-4 level and advanced approximately 5 cm into the epidural space. Anaesthesia was induced with 5 mg kg⁻¹ thiopentone iv, and 0.2 mg kg⁻¹ vecuronium iv was used to facilitate tracheal intubation. After tracheal intubation, anaesthesia was maintained with nitrous oxide 66% and isoflurane 0.5%-2.0% (inspired concentration) in oxygen. No patient received an opioid before tracheal intubation or during maintenance of anaesthesia. A nasogastric tube was inserted and suction applied to empty the stomach of air and other contents. Ventilation was controlled mechanically and was adjusted to maintain an expired PETCO₂ between 35 mmHg and 40 mmHg with an anaesthetic/respiratory gas analyzer (Capnomac Ultima, Datex, Finland). When haemodynamic variables were stable, 10-15 ml lidocaine 1.5% were injected through the epidural catheter. Muscle relaxants were used as required. At the end of surgery, 0.02 mg kg⁻¹ atropine iv and 0.04 mg kg⁻¹ neostigmine iv were administered for reversal of muscle relaxation, and the trachea was extubated. After tracheal extubation, the nasogastric tube was again suctioned and then removed. Rectal temperature was monitored and maintained at 37±1°C. If two or more episodes of PONV occurred during the first 24 hr after anaesthesia, another rescue antiemetic (e.g., domperidone) was given. For postoperative analgesia, a continuous epidural infusion with a mixture of 40 ml bupivacaine 0.25% and 0.1 mg kg⁻¹ morphine was started after the end of surgery at a rate of 1.7 ml hr⁻¹ (Drug infusion balloon catheter, Dib International, Japan). Patients in all groups were also allowed to receive indomethacin (50 mg, pr) when they complained of pain.

Postoperatively, all episodes of PONV experienced by the patients during the first 24 hr after anaesthesia were recorded by nursing staff without knowledge of which antiemetics the patients had received. Nausea was defined as the subjectively unpleasant sensation associated with awareness of the urge to vomit, whereas vomiting was defined as the forceful expulsion of gastric contents from the mouth. Retching was defined as the laboured, spasmodic, rhythmic contraction of the respiratory muscle without the expulsion of gastric content, and was also classified as vomiting. The details of any adverse event throughout the study were also recorded either by follow-up nurses who interviewed the patients or by spontaneous complaints of them.

Patient demographic data were analysed with oneway analysis of variance (ANOVA) and Student's t test. The incidence of PONV and adverse events was compared with nonparametric tests (χ², Kruskall-Wallis). A P < 0.05 was regarded as statistically significant. All values were expressed as mean ± SD or number.

Results
Patient demographics, including age, height, weight, history of motion sickness or previous PONV, duration of operation or anaesthesia and analgesics used postoperatively, and types of operation performed were not different among the groups (Table I).