# The Effect of Timing of Dexamethasone Administration on Its Efficacy as a Prophylactic Antiemetic for Postoperative Nausea and Vomiting

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We evaluated the timing effect of a 10-mg IV administration of dexamethasone on its efficacy as a prophylactic antiemetic on postoperative nausea and vomiting (PONV). One hundred twenty women ($n = 40$ in each of three groups) undergoing abdominal total hysterectomy under general anesthesia were enrolled in this randomized, double-blinded, placebo-controlled study. Group 1 received dexamethasone before the induction of anesthesia, Group 2 received dexamethasone at the end of anesthesia, and Group 3 received placebo (saline). The incidence of PONV was evaluated. During the postoperative period of 0–2 h, patients in Group 1 reported a less frequent incidence of PONV (15%) than those in Groups 2 and 3 (45% and 53%, respectively). Patients in Group 1 also requested less rescue antiemetic (8%) than those in Groups 2 and 3 (30% and 35%, respectively). During the postoperative period of 2–24 h, patients in both Groups 1 and 2 reported less frequent incidences of PONV (25% and 28%) and requested fewer rescue antiemetics (13% and 15%) than those in Group 3 (55% and 38%, respectively). In conclusion, the prophylactic IV administration of dexamethasone immediately before the induction, rather than at the end of anesthesia, was more effective in preventing PONV.

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Dexamethasone is effective in reducing the incidence of postoperative nausea and vomiting (PONV) in patients undergoing adenotonsillectomy, thyroidectomy, cholecystectomy, and abdominal hysterectomy (1–11). Despite this antiemetic effect, the optimal timing of dexamethasone administration on its efficacy as a prophylactic antiemetic on PONV has not been previously studied. We designed this study to test the hypothesis that dexamethasone is more effective in preventing PONV when administered before the induction of anesthesia versus at the end of anesthesia.

## Methods

The protocol was approved by our Hospital Committee for Human Investigation and informed consent was obtained from each patient. One hundred twenty adult female patients, ASA physical status I and II, between the ages of 35 and 45 yr, scheduled for abdominal total hysterectomy under general anesthesia were enrolled in this randomized, double-blinded, placebo-controlled study. Patients with a history of motion sickness or gastrointestinal disorders and those who had received antiemetics within 48 h before surgery were excluded. Before the study, patients provided detailed medical histories and demographic information, including age, weight, height, drug consumption, and last menstrual period.

In the preoperative holding area, patients were allocated randomly to one of three groups ($n = 40$ each) by using a computer-generated random number table. At 1 min before the induction of anesthesia, Group 1 received 10 mg (2 mL) of IV dexamethasone, whereas Groups 2 and 3 received 2 mL of IV saline. At the end of the administration of anesthesia, after tracheal extubation, Group 2 received 10 mg of IV dexamethasone, whereas Groups 1 and 3 received 2 mL of IV saline. The randomized process and the identity of the study drug were blinded from the patients, the anesthesiologists

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during surgery, and the investigators who collected the postoperative data.

The anesthetic technique and surgical procedures were identical in all patients. Anesthesia was induced with 2–2.5 mg/kg IV propofol, 0.2 mg of IV glycopyrrolate, and 2 μg/kg IV fentanyl. Tracheal intubation was facilitated by the administration of 0.15 mg/kg IV vecuronium. Anesthesia was maintained with 1.0% to 2.5% isoflurane (inspired concentration) in oxygen. Supplemental analgesia was provided with 50- to 100-μg IV boluses of fentanyl. Abdominal total hysterectomy (with or without oophorectomy) was performed in all patients. At the cessation of the surgery, 0.6 mg of IV glycopyrrolate and 3 mg of IV neostigmine were administered for reversal of muscle relaxation, and the trachea was extubated.

After surgery, patients were immediately transported to the postanesthetic care unit (PACU) where patients were observed for 24 h. During their stay in the PACU (2 h), vital signs, such as blood pressure, heart rate, and respiratory rate, were monitored every 15 min and oxygen saturation was monitored continuously. Patients were transferred to a ward for further observation 2 h later.

Pain intensity was rated by patients by using the visual analog scale (VAS; 0 = no pain, 10 = most severe pain) at 1- h intervals during their stay in PACU and at 4-h intervals in the ward (except during sleep). When a patient complained of pain and requested analgesia, 2 mg of IV of morphine was given and was repeated to achieve patient comfort; then, a patient-controlled analgesia (PCA) pump was programmed to deliver 1 mg of IV morphine on demand with a lockout interval of 10 min. The consumption of PCA morphine was recorded.

Nausea and vomiting were assessed immediately after surgery and at 30-min intervals in the PACU for 2 h. In addition, nausea and vomiting were evaluated every 4 h (except during sleep) by direct questioning or by spontaneous complaint of the patients. Nausea and vomiting were evaluated on a 3-point ordinal scale (0 = none, 1 = nausea, and 2 = vomiting). No distinction was made between vomiting and retching (i.e., a retching event was considered as a vomiting event). When vomiting occurred or by patient's request, 1.25 mg of IV droperidol was given.

Sample size was predetermined. We expected a 30% difference among groups in the proportion of patients requiring rescue IV droperidol for nausea or vomiting. The $\alpha$ error was set at 0.05 (two-sided) and the $\beta$ error at 0.10. Analysis showed that 40 patients per group would be sufficient (12). A series of one-way analyses of variance was conducted to examine differences among the three study groups with respect to parametric variables. If a significant difference was found, the Bonferroni *t*-test was used to detect the intergroup differences. The Kruskal-Wallis test was used to determine differences among the three groups with respect to nonparametric variables, followed by the Mann-Whitney ranked sum test for intergroup differences. Categorical variables were analyzed by using a series of $3 \times 2$ $\chi^2$ tests to determine differences among the three groups, followed by $2 \times 2$ $\chi^2$ tests for intergroup differences. All follow-up analyses were corrected for the number of simultaneous contrasts by using the Bonferroni adjustments. A $P < 0.05$ was considered significant.

## Results

All 120 patients completed the study. There were no significant differences among the three groups with respect to age, weight, height, last menstrual period, types of surgery, duration of anesthesia and surgery, and the total of perioperative fentanyl doses (Table 1).

No patient demonstrated arterial oxygen saturation <90%. Patients in the three groups consumed similar amounts of morphine and reported similar VAS pain scores (0–2 h, Table 2). During their stay in the ward (2–24 h), the total consumption of PCA morphine was 15, 14, and 17 mg (median) in Groups 1, 2, and 3, respectively, and the VAS pain scores were 1.9, 2.1, and 2.3 (median) in Groups 1, 2, and 3, respectively.

Because both nausea and vomiting present the same unpleasant physical reaction, the only difference being the severity, we used a total incidence of nausea and vomiting to present PONV (Table 3). The percent of patients requesting rescue antiemetics in each group was also calculated. During their stay in PACU (0–2 h postoperatively), patients in Group 1 reported a significantly less frequent incidence of PONV and requested less rescue antiemetics than those in Groups 2 and 3 (Table 3). During the observatory period of 2–24 h (in the ward), patients in both Groups 1 and 2 reported a significantly less frequent incidence of PONV and requested less rescue antiemetics than those in Group 3 (Table 3).

## Discussion

Although dexamethasone is effective in preventing PONV associated with a surgical procedures (1–11), the optimal timing of its administration for its efficacy as a prophylactic antiemetic on PONV has not been studied. We demonstrated that dexamethasone, when administered immediately before the induction of anesthesia, provided an effective antiemetic effect throughout the first 24 hours of the postoperative period. On the contrary, when administered at the end of anesthesia, dexamethasone did not provide an effective antiemetic effect during the immediate postoperative period of 0–2 hours. Because more than one half of the patients experienced PONV in this early

**Table 1.** Demographic Data

| | Group 1 (preinduction) | Group 2 (end of anesthesia) | Group 3 (placebo) |
|---|---|---|---|
| *n* | 40 | 40 | 40 |
| Age (yr) | 42 (36–44) | 41 (35–45) | 39 (35–43) |
| Weight (kg) | 54 (42–71) | 56 (46–75) | 54 (41–69) |
| Height (cm) | 157 (139–171) | 158 (141–168) | 156 (138–170) |
| Last menstrual period (days) | | | |
| 0–8 | 12 | 12 | 14 |
| 9–16 | 9 | 12 | 14 |
| 16–28 | 12 | 11 | 8 |
| >28 | 7 | 5 | 4 |
| Abdominal total hysterectomy (with/without oophorectomy) | 6/34 | 5/35 | 3/37 |
| Duration of anesthesia (min) | 136 (110–178) | 142 (115–183) | 145 (121–162) |
| Duration of surgery (min) | 108 (82–148) | 121 (91–152) | 119 (86–143) |
| Total doses of perioperative fentanyl ($\mu$g) | 250 (150–400) | 300 (200–450) | 300 (150–450) |

Values are *n* or median (range).
No significant differences among groups.

**Table 2.** Postoperative VAS Pain Scores and Morphine Consumption of Patients During Their Stay in the Postanesthetic Care Unit

| | VAS score | | | Morphine consumption | | |
|---|---|---|---|---|---|---|
| Time (h) | Group 1 (preinduction) | Group 2 (end of anesthesia) | Group 3 (placebo) | Group 1 (preinduction) | Group 2 (end of anesthesia) | Group 3 (placebo) |
| 1 | 3.5 (2.3–5.6) | 3.8 (2.2–6.5) | 3.9 (2.5–6.5) | 12 (4–21) | 10 (6–15) | 14 (7–22) |
| 2 | 2.7 (1.8–4.8) | 3.0 (1.9–5.2) | 3.1 (1.8–5.3) | 2 (0–5) | 3 (0–6) | 3 (0–6) |

Values are median (range).
VAS = visual analog scale.
No significant differences among groups.

**Table 3.** Incidence of Nausea and Vomiting after Abdominal Total Hysterectomy

| | Group 1 (preinduction) | Group 2 (end of anesthesia) | Group 3 (placebo) | *P** (Group:Group) |
|---|---|---|---|---|
| In the PACU (0–2 h postoperatively) | | | | |
| Nausea | 4 (10) | 10 (25) | 13 (33) | |
| Vomiting | 2 (5) | 8 (20) | 8 (20) | |
| Total | 6 (15) | 18 (45) | 21 (53) | 1:2<0.01,1:3<0.001 |
| Rescue antiemetics | 3 (8) | 12 (30) | 14 (35) | 1:2<0.05,1:3<0.01 |
| In the ward (2–24 h postoperatively) | | | | |
| Nausea | 6 (15) | 7 (18) | 12 (30) | |
| Vomiting | 4 (10) | 4 (10) | 10 (25) | |
| Total | 10 (25) | 11 (28) | 22 (55) | 1:3<0.05,2:3<0.05 |
| Rescue antiemetics | 5 (13) | 6 (15) | 15 (38) | 1:3<0.05,2:3<0.05 |

Values are number of patients (%). $n = 40$ for each group.
PACU = postanesthetic care unit.
*$P$ value using $3 \times 2$ $\chi^2$ test followed by $2 \times 2$ $\chi^2$ test.

postoperative period (53%, as shown in the placebo group), it is very important that a prophylactic antiemetic should be effective during this period.

Because dexamethasone may have a delayed onset of action, we questioned how much time is required for dexamethasone to initiate its antiemetic effect. After conducting an extensive literature search, we were unable to find a report that mentioned the onset time of a dexamethasone antiemetic effect. After a comparison study design, we found dexamethasone was not effective during zero to two hours after the administration (as shown in Group 2); however, it proved to be effective in the following period (as shown in Groups 1 and 2). Therefore, we suggest the onset time of dexamethasone's antiemetic effect may be approximately two hours.

We did not examine the duration of dexamethasone's antiemetic effect. In previous studies, IV dexamethasone had a prolonged antiemetic effect of at least 24 h in patients undergoing clinical surgical procedures (1–11).

The etiology of PONV in patients undergoing abdominal total hysterectomy is not fully understood. Risk factors, such as a difference in the phase of menstrual cycle, intraoperative use of isoflurane, fentanyl, and glycopyrrolate; postoperative pain; and the use of morphine, may all contribute to these episodes (13–15). Because these risk factors could have interfered with the interpretation of the study result, we controlled for each within the study design. All patients underwent abdominal total hysterectomy with a standardized anesthetic regimen and surgical procedure. As predicted, the duration of anesthesia, surgery, and the anesthetics used were similar among groups. In addition, the phase of menstrual cycle, the intensity of postoperative pain, and use of morphine were similar among groups. Therefore, the differences in the incidence of PONV among groups are probably attributable to the timing of dexamethasone administration, rather than to any confounding variable.

Although the minimum effective dose of dexamethasone for the prevention of PONV was suggested to be 2.5 mg in a recent study (16), a 8- to 10-mg dose of dexamethasone was most frequently used (1–11). Therefore, we used a 10-mg dose.

In conclusion, the prophylactic administration of 10 mg of IV dexamethasone, immediately before the induction of anesthesia, was more effective than at the end of anesthesia for preventing PONV in patients undergoing abdominal total hysterectomy.

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