Low-dose dexamethasone effectively prevents postoperative nausea and vomiting after ambulatory laparoscopic surgery

[Une faible dose de dexaméthasone prévient efficacement les nausées et les vomissements postopératoires en chirurgie laparoscopique ambulatoire]

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Purpose: To evaluate the prophylactic effect of low-dose dexamethasone (5 mg) on postoperative nausea and vomiting (PONV) in women undergoing ambulatory laparoscopic surgery. Metoclopramide and saline served as controls.

Methods: One hundred twenty women (n=40 in each of the three groups) undergoing ambulatory laparoscopic tubal ligation under general anesthesia were enrolled in this randomized, double-blinded, placebo-controlled study. After tracheal intubation, group I received *iv* dexamethasone 5 mg, whereas groups II and III received *iv* metoclopramide 10 mg and saline, respectively.

Results: Patients in group I reported a lower incidence of PONV and requested less rescue antiemetics than those in group III during the first four postoperative hours (P <0.01). Patients in group I reported a lower incidence of PONV than those in groups II (P <0.05) and III (P <0.01) during the 24-hr postoperative period. Groups II and III did not differ from each other in the incidence of PONV and the proportion of patients who requested rescue antiemetics.

Conclusion: Prophylactic *iv* dexamethasone 5 mg significantly reduces the incidence of PONV in women undergoing ambulatory laparoscopic tubal ligation. At this dose, dexamethasone is more effective than metoclopramide 10 mg or placebo.

Objectif : *Évaluer l'effet prophylactique d'une faible dose de dexaméthasone (5 mg) sur les nausées et vomissements postopératoires (NVPO) chez des patientes de chirurgie laparoscopique ambulatoire. Le métoclopramide et une solution salée ont servi de témoins.*

Méthode : *Cent vingt femmes (n = 40 dans chacun des trois groupes formés de façon aléatoire), devant subir une ligature des trompes sous anesthésie générale en chirurgie laparoscopique ambulatoire, ont participé à l'étude randomisée, en double insu et contrôlée contre placebo. Après l'intubation endotrachéale, les patientes du groupe I ont reçu 5 mg de dexaméthasone iv tandis que celles des groupes II et III ont reçu 10 mg de métoclopramide ou de solution salée iv, respectivement.*

Résultats : *Les patientes du groupe I ont signalé une plus faible incidence de NVPO et ont demandé moins d'antiémétiques de secours que les patientes du groupe III pendant les quatre premières heures postopératoires ($P < 0,01$). Les patients du groupe I ont eu moins de NVPO que celles des groupes II ($P < 0,05$) et III ($P < 0,01$) pendant une période de 24 h après l'intervention. Aucune différence intergroupe quant à l'incidence de NVPO et au nombre de patientes qui ont eu recours aux antiémétiques n'a été notée entre les patientes des groupes II et III.*

Conclusion : *L'administration iv de 5 mg de dexaméthasone réduit significativement l'incidence de NVPO chez des patientes qui subissent une ligature des trompes en chirurgie laparoscopique ambulatoire. C'est plus efficace que 10 mg de métoclopramide ou de placebo.*

POSTOPERATIVE nausea and vomiting (PONV) is among the most unpleasant experiences associated with ambulatory surgery.[1–4] The incidence of nausea and vomiting after outpatient gynecological laparoscopic surgery is particularly high, with previous reported rates of 54–92%.[1–5] In an attempt to decrease the incidence of PONV in the ambulatory setting, a number of antiemetics have been studied.[1–6] Among the

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antiemetics currently used, 5 HT_3 antagonists such as ondansetron and granisetron are increasing in popularity. Although the antiemetics are effective, the high cost of these drugs limits their widespread use.[1,3,4] Other currently used antiemetic drugs (e.g., anticholinergics, dopamine receptor antagonists, antihistamines), although effective, possess clinically significant side effects (e.g., restlessness, dry mouth, tachycardia, and extrapyramidal symptoms).[6–8] A low cost antiemetic agent with few side effects would be of benefit to anesthesiologists and their patients.

Since 1981, dexamethasone has been reported to be effective in reducing the incidence of emesis in patients undergoing chemotherapy.[9–11] Recently, dexamethasone has also been reported to be effective in reducing the incidence of PONV.[12–16] The commonly used dose is 8–10 mg but the minimum effective dose is suggested to be 5 mg for the prevention of PONV in patients undergoing thyroidectomy.[16] The aim of the present study was to evaluate the prophylactic antiemetic effect of low-dose dexamethasone (5 mg) in women undergoing ambulatory laparoscopic tubal ligation. Metoclopramide, a commonly used antiemetic,[2] and saline were used as controls.

Patients and methods

After obtaining Institutional Review Board approval and written informed consent from the patients, 120 women, ASA physical status I or II, scheduled for outpatient laparoscopic tubal ligation, were enrolled in the study. Patients who were breast feeding, weighed >90 kg, or who had a history of PONV, motion sickness, or had received an antiemetic within 24-hr before surgery were excluded from participation. Patients provided detailed medical histories and demographic information, including age, weight, height, drug consumption, as well as last menstrual period.

On arrival in the operating room, routine monitoring devices were placed, and baseline blood pressure, heart rate, and pulse oximetry values were recorded. Patients were, then, randomly assigned into one of the three groups (n=40, each) using a computer generated random number table. Study medications totaled 2 mL, were prepared by one of the investigators and were administered in a double-blind fashion. After tracheal intubation, group I received *iv* dexamethasone 5 mg, group II received *iv* metoclopramide 10 mg, while group III received *iv* saline. The anesthetic technique and surgical procedure were identical in all patients. Anesthesia was induced with *iv* propofol (2–2.5 $mg \cdot kg^{-1}$), glycopyrrolate (0.2 mg) and fentanyl (2 $\mu g \cdot kg^{-1}$). Tracheal intubation was facilitated with *iv* vecuronium (0.15 $mg \cdot kg^{-1}$). Anesthesia was maintained with 1.0–2.5% (inspired concentration) isoflurane in oxygen. Ventilation was controlled mechanically and was adjusted to keep an end-tidal concentration of CO_2 between 30 and 40 mmHg with an anesthetic/respiratory gas analyzer (Capnomac Ultima; Datex, Helsinki, Finland). Laparoscopic tubal ligation was performed under video guidance and involved two punctures of the abdomen. During surgery, the patients were placed in a Trendelenburg position and the abdomen was insufflated with CO_2 to an intra-abdominal pressure of 10–14 mmHg. At the cessation of the surgery, *iv* glycopyrrolate (0.6 mg) and neostigmine (3 mg) were administered for reversal of neuromuscular blockade, and the trachea was extubated.

After surgery, patients were transported to the postanesthetic care unit (PACU). During their stay in PACU (four hours), vital signs such as blood pressure, heart rate, and respiratory rate were monitored every 15 min and oxygen saturation (SaO_2; by pulse oximetry) was monitored continuously. Tenoxicam 20 mg *iv* was given routinely for the prevention of postoperative pain. Pain intensity was assessed by using a 10-cm visual analog scale (VAS; 0=no pain to 10=most severe pain). Because pain after laparoscopic tubal ligation is relatively minor,[17] patients did not receive further analgesic treatment after discharge.

Nausea and vomiting were assessed immediately after operation and at one-hour intervals in the PACU for four hours. In addition, nausea and vomiting were assessed by telephone 24-hr after hospital discharge. Nausea and vomiting were evaluated on a 3-point ordinal scale (0=none, 1=nausea, and 2=vomiting). In the current study, no distinction was made between vomiting and retching (i.e., a retching event was considered a vomiting event). In the PACU, *iv* ondansetron 4 mg was given at the patient's request (for relief of intolerable nausea, a subjective feeling which was reported by patients) or when vomiting occurred. No nausea, no vomiting and no antiemetic medication during the 24-hr postoperative period was defined as successful protection. The patients and the investigator who collected the data were blinded to the patient's group. Side effects, e.g., extrapyramidal symptoms, if present, were recorded.

Sample size was predetermined by using a power analysis based on the assumptions that (a) the total incidence of nausea and vomiting in the saline group would be 60%,[14] (b) a 40% reduction in the total incidence of nausea and vomiting (from 60% to 36%) in the treatment group would be of clinical relevance, and (c) α=0.05, ß=0.2. The analysis showed that 37 patients per group would be sufficient. A series of one-way analyses of variance were 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 rank-sum test for intergroup differences. Categorical variables were analyzed by using a series of 3 x 2 χ^2 test to determine the differences among the three groups, followed by 2 x 2 χ^2 test for intergroup differences. All follow-up analyses were corrected for the number of simultaneous contrasts using the Bonferroni adjustments. A P value <0.05 was considered significant.

Results

Of the 120 patients enrolled in this study, three patients who did not complete the surgical procedure (laparoscopic tubal ligation) due to intra-abdominal adhesions and two patients who could not be contacted by telephone after hospital discharge were eliminated from the study. The data obtained from the remaining 115 patients were analyzed. The patients' characteristics (e.g., age, weight, and height), interval since the last menstrual period and the durations of anesthesia and surgery were similar among the groups (Table I).

In the PACU, vital signs such as blood pressure, heart rate, and respiratory rate were stable and were not different among the groups. No patients demonstrated a SaO_2 below 90%. The intensity of postoperative pain was relatively minor, patients in the three groups reporting a similar low VAS pain score (median; group I=1.5; group II=2.1; group III=2.1).

The efficacy of dexamethasone as a prophylactic antiemetic compared with placebo is summarized in Table II. We used the total incidence of nausea and vomiting to present PONV. During their stay in the PACU (zero to four hours postoperatively), patients in group I reported a lower incidence of PONV than those in group III (P <0.01; Table II). In addition, less patients in group I requested a rescue antiemetic (*iv* ondansetron 4 mg) than in group III (P <0.01). During the total observation period 0–24 hr , patients in group I reported a lower incidence of PONV and a higher percentage of successful protection than those in groups II and III (P <0.05, P <0.01, respectively). Groups II and III did not differ from each other in the incidence of PONV, antiemetic medication and successful protection. Side effects related to the use of dexamethasone and metoclopramide were not found.

TABLE I Patients' characteristics

	Dexamethasone (Group I)	*Metoclopramide (Group II)*	*Saline (Group III)*
No.	39	38	38
Age (yr)	32 (27–35)	34 (31–36)	35 (30–37)
Weight (kg)	54 (42–72)	56 (46–75)	56 (45–76)
Height (cm)	158 (145–172)	157 (138–170)	156 (139–173)
Interval since last menstrual period (days)			
0–8	12	11	11
9–16	7	9	10
16–28	11	12	9
>28	9	6	8
Duration of anesthesia (min)	65 (45–78)	68 (49–78)	64 (51–76)
Duration of surgery (min)	41 (32–63)	45 (38–65)	42 (38–64)

Values given as numbers or median (range).

TABLE II Incidence of nausea and vomiting after laparoscopic tubal ligation

	Dexamethasone (Group I)	*Metoclopramide (Group II)*	*Saline (Group III)*
No.	39	38	38
In the PACU (0-4 hr postoperatively)			
- Nausea	6 (15)	8 (21)	12 (32)
- Vomiting	3 (8)	6 (16)	10 (26)
- Total	9 (23)†	14 (37)	22 (58)
- Rescue antiemetic	4 (10)†	10 (26)	16 (42)
After discharge (4-24 hr postoperatively)			
- Nausea	4 (10)	6 (15)	8 (21)
- Vomiting	1 (3)	4 (11)	3 (8)
- Total	5 (13)	10 (26)	11 (29)
From 0-24 hr postoperatively			
- Nausea	8 (21)	12 (32)	13 (34)
- Vomiting	3 (8)	8 (21)	11 (29)
- Total	11 (28)*†	20 (53)	24 (63)
Successful protection	28 (72)*†	18 (47)	14 (37)

Values are numbers of patients (%). PACU=postanesthetic care unit. Successful protection was defined as no nausea, no vomiting and no antiemetic medication.*P <0.05 when compared with group II; †P <0.01 when compared with group III using 3 x 2 χ^2 test followed by 2 x 2 χ^2 test.

Discussion

Although the use of laparoscopy for tubal ligation has decreased surgical morbidity and has become a popular procedure in an ambulatory setting,[18,19] a high incidence of PONV (54–92%) has been reported.[1–5] In our study, we found that the total incidence of PONV was 63% within 24-hr postoperatively in patients undergoing laparoscopic tubal ligation when no antiemetic was given prophylactically. After pretreatment with low-dose of dexamethasone 5 mg, the incidence of PONV was reduced to 28%. We also

found that dexamethasone 5 mg was more effective than metoclopramide 10 mg and saline in preventing PONV in women undergoing ambulatory laparoscopic tubal ligation.

Several studies have demonstrated dexamethasone's efficacy and minimal adverse events in the prevention of nausea and vomiting associated with chemotherapy.[9–11] Dexamethasone has also been found to be effective in the prevention of PONV.[12–16] Among the doses used, 8–10 mg dexamethasone has been used most frequently in the prevention of PONV.[12–15] Although a 2.5-mg dose was suggested to be the minimum effective dose for PONV in patients undergoing major gynecologic surgery,[20] it was only partially effective for this purpose in patients undergoing thyroidectomy.[16] A 5-mg dose was found to be effective in both situations.[16,20] Therefore, a 5 mg dose of dexamethasone was chosen in the present study.

The etiology of PONV in patients undergoing laparoscopic tubal ligation is not fully understood. Risk factors such as a residual pneumoperitoneum after CO_2 insufflation,[21] intraoperative use of isoflurane and fentanyl,[8,22] appearance of postoperative pain,[8,17,22] and difference in the phase of menstrual cycle[5] may all contribute to these episodes. In the present study, all of these factors were controlled by study design. All patients underwent laparoscopic tubal ligation with a standardized surgical procedure and anesthetic regimen. As predicted, the duration of surgery, anesthesia and the anesthetics used were similar among the groups. In addition, the phase of menstrual cycle and the intensity of postoperative pain were also similar among the groups. Therefore, it is likely the differences in the incidence of PONV among the groups can be attributed to the study drugs rather than to any confounding variable.

Surprisingly, metoclopramide 10 mg did not prevent the occurrence of PONV and did not reduce the proportion of patients who requested rescue antiemetics. Metoclopramide, a dopamine and serotonin receptor antagonist, was discovered almost 40 years ago and is known as an antiemetic since the 1960s.[2,7,23] It is still used widely in clinical practice. Metoclopramide 10 mg *iv* is suggested to be the optimal dose for PONV, although much higher doses have been used for the prevention of chemotherapy-related emesis.[23] Recently, a systematic review of metoclopramide stated that the drug does not protect against nausea or late vomiting.[23] The anti-vomiting effect of metoclopramide appears to be present only during the first six hours following administration.[23] In the present study, metoclopramide was administered at the beginning of surgery for the evaluation of its prophylactic antiemetic properties and was found to reduce PONV by 21% when compared to saline during the first four hours postoperatively (around five hours after administration). However, the difference was not significant. This result may be explained by its relatively weak antiemetic effect.

Side effects related to the use of dexamethasone and metoclopramide were not found. Multiple-dose corticosteroid therapy (> one week) may cause side effects, such as increased risk of infection, glucose intolerance, delayed wound healing, superficial ulceration of the gastric mucosa, etc.[24] However, these side effects are not found after a single dose of dexamethasone 8–10 mg.[12–16] In our study, a single and relative low-dose of dexamethasone 5 mg were used and no discernible side effects were found. Metoclopramide-related side effects, such as extrapyramidal symptoms, have been reported. However, the incidence is very low (<1%).[7,23] In our study, no metoclopramide-related extrapyramidal symptoms were found.

Cost is an ever-increasing concern in today's health care system. Both of the prophylactic antiemetics we used are relatively inexpensive. Dexamethasone 5 mg costs $18 new Taiwan dollars (NT), whereas metoclopramide 10 mg costs $5 NT. This is remarkably less expensive than a similar and effective dose of an alternate antiemetic, ondansetron, which costs $450 NT for a 4-mg dose. This is why ondansetron was not chosen as our first-line prophylactic antiemetic.

In summary, prophylactic *iv* administration of low-dose dexamethasone 5 mg significantly reduced the incidence of PONV in women undergoing ambulatory laparoscopic tubal ligation. It was more effective than metoclopramide 10 mg *iv or* placebo. Dexamethasone 5 mg appears to be a cost-effective alternative for the prevention of PONV in women undergoing ambulatory laparoscopic tubal ligation.

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