Dexamethasone for prophylaxis of nausea and vomiting after epidural morphine for post-Caesarean section analgesia: comparison of droperidol and saline

J. I. Tzeng[1 2], J. J. Wang[2 4], S. T. Ho[2], C. S. Tang[1], Y. C. Liu[3] and S. C. Lee[3]*

[1]*Department of Anaesthesiology, School of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.*
[2]*Department of Anaesthesiology and* [3]*Department of Surgery, Tri-Service General Hospital, Taipei, Taiwan.*
[4]*Department of Anaesthesiology, Chi-Mei Medical Center, Tainan, Taiwan*

**Corresponding author: Department of Surgery, Tri-Service General Hospital/National Defense Medical Center, Rm 8113, No. 161, Sec. 6, Minchuan E. Rd., Taipei, Taiwan*

We have evaluated the prophylactic effect of i.v. dexamethasone 8 mg in preventing nausea and vomiting during epidural morphine for post-Caesarean section analgesia. Droperidol 1.25 mg and saline served as the control. We studied 120 parturients (n=40 in each group) receiving epidural morphine for post-Caesarean section analgesia, in a randomized, double-blind, placebo-controlled study. All parturients received epidural morphine 3 mg. Both dexamethasone and droperidol significantly decreased the total incidence of nausea and vomiting compared with saline, with incidences of 18, 21 and 51% for the three treatments respectively (P<0.01 and P<0.05 respectively). Parturients who received droperidol reported a more frequent incidence of restlessness (16%) than those who received dexamethasone (P<0.05).

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Epidural morphine has a potent and long-acting analgesic effect on postoperative pain.[1–5] It is very convenient for clinical use and is widely accepted for analgesia after Caesarean section.[5–8] However, high incidences of nausea and vomiting (30–65%) have been reported.[9–11] Among the antiemetics used currently, 5-HT_3 antagonists (e.g. ondansetron, granisetron) possess good efficacy, but cost limits their use.[12–15] Dopamine receptor antagonists (e.g. droperidol, prochorperazine, metoclopramide) are commonly used but are associated with a variety of extrapyramidal symptoms.[16 17] Antihistaminic and anticholinergic drugs (e.g. scopolamine, hydroxyzine, promethazine) are also effective, but excessive sedation and tachycardia may occur.[9 18 19]

Dexamethasone is an effective antiemetic after single-dose administration.[11–15 20–23] It is effective in preventing chemotherapy-related emesis and postoperative nausea and vomiting (PONV).[12–15 20–23] Recently, it has also been found to be effective in preventing nausea and vomiting related to epidural morphine in patients undergoing abdominal hysterectomy.[11] We conducted a randomized, double-blinded and placebo-controlled study to evaluate whether dexamethasone was also effective in preventing nausea and vomiting after epidural morphine for post-Caesarean section analgesia.

Patients and methods

The protocol was approved by the Hospital Committee for Human Investigation and informed consent was obtained from each parturient. One hundred and twenty parturients (ASA I–II; 20–35 yr) scheduled for elective Caesarean section under epidural anaesthesia were enrolled in this randomized, double-blind, placebo-controlled study.

No premedication was given. Surgical analgesia to T_4 dermatome level was provided by a dose of 2% lignocaine 15–18 ml (with 1:100 000 epinephrine), followed by intermittent small-dose injections of 2% lignocaine (with epinephrine) as necessary through an epidural catheter in the L3–4 or L4–5 interspace. Lactated Ringer's solution 500 ml was given i.v. before surgery. After delivery of the baby, 10 units of i.v. oxytocin and 0.2 mg of i.m. ergonovine were given to all parturients. Estimated fluid deficit and maintenance requirements were replaced with lactated Ringer's solution i.v. During surgery, i.v. midazolam 2.5 mg was

given for sedation after delivery of the baby; no supplementary analgesic was given.

Before surgery, a randomization table was used to assign parturients to one of three groups (n=40 for each group). At the end of surgery, the dexamethasone group received i.v. dexamethasone 8 mg (2 ml), the droperidol group received i.v. droperidol 1.25 mg (2 ml) and the saline group received i.v. saline (2 ml). One minute later, all parturients received 3 mg of preservative-free morphine in 10 ml of normal saline through the epidural catheter for postoperative analgesia. The randomization process and the identity of the study drugs were blinded from the parturients, the anaesthetists during surgery and the investigators who collected the postoperative data.

The incidences of nausea and vomiting were recorded for 24 h. Nausea was defined as a subjectively unpleasant sensation associated with awareness of the urge to vomit; vomiting was the forceful expulsion of gastric contents from the mouth. Nausea and vomiting were evaluated on a 3-point ordinal scale (0=none, 1=nausea, 2=vomiting). The total incidence of nausea and vomiting was calculated. Metoclopramide 10 mg i.v. was available when vomiting occurred or on request. The proportion of parturients requiring rescue antiemetic in each group was recorded.

Pain intensity was assessed with a 10-cm visual analogue scale (VAS; 0=no pain, 10=most severe pain) and was recorded between 8:00 a.m. and 10:00 p.m. If parturients requested rescue analgesia for pain control, i.m. diclofenac 75 mg was available. Pruritus was assessed on a 3-point ordinal scale (0=none, 1=pruritus but only in a small area of the body, 2=generalized pruritus). Pruritus was treated with i.m. diphenhydramine (20 mg every 4 h as needed). Restlessness was also evaluated;[16] it was defined as a sensation of nervousness with an inability to keep still. Restlessness was treated with i.m. diphenhydramine 20 mg. The occurrence of any side-effect accompanying dexamethasone usage, such as wound infection or delayed wound healing, was recorded.

Sample size was predetermined.[24] We expected a 30% difference among groups in the proportion of parturients requiring rescue antiemetic for nausea and/or vomiting.[9–11] The α error was set at 0.05 (two-sided) and the β error at 0.10. The analysis showed that 37 parturients per group would be sufficient.[24] A series of one-way analyses of variance were conducted to examine differences among the three 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 non-parametric variables, and was followed by the Mann–Whitney rank-sum test for intergroup differences. Categorical variables were analysed with a series of 3×2 χ^2 tests to determine differences among the three groups, followed by a 2×2 χ^2 test for intergroup differences. All follow-up analyses were corrected for the number of simultaneous contrasts using Bonferroni adjustment. A P value less than 0.05 was considered significant.

Results

Of the 120 parturients enrolled, seven were withdrawn because of failure of epidural catheterization before surgery. Therefore, 113 parturients completed the trial. There was no significant difference among groups with respect to age, weight, height, parity, duration of anaesthesia and surgery, and lignocaine consumption during surgery (Table 1).

After surgery, all parturients received epidural morphine for postoperative pain relief. During the 24-h observation period, 8 parturients in the dexamethasone group and 9 and 11 in the droperidol and saline groups respectively requested rescue analgesia (i.m. diclofenac 75 mg). The number of diclofenac injections was 10 in the dexamethasone group, and 11 and 14 in the droperidol and saline groups respectively. The median time until rescue analgesia was 16 h in the dexamethasone group and 14 h in both the droperidol and the saline group. The differences in the above variables among groups were not significant. All parturients reported low VAS pain scores (0–3) and the differences among groups were not significant.

The total incidence of nausea and vomiting was 18% in the dexamethasone group and 21% in the droperidol group, in comparison with 51% in the saline group (P<0.01 and P<0.05 respectively) (Table 2). The proportions of

Table 1 Patient characteristics. Values are median (range)

Characteristic	Group		
	Dexamethasone (n=38)	**Droperidol (n=38)**	**Saline (n=37)**
Age (yr)	31 (20–35)	33 (23–35)	32 (21–35)
Weight (kg)	70 (52–86)	72 (52–89)	71 (51–88)
Height (cm)	158 (140–172)	158 (143–174)	157 (142–176)
Parity	2 (1–3)	2 (1–3)	2 (1–3)
Duration of anaesthesia (min)	64 (48–83)	58 (49–84)	61 (52–87)
Duration of surgery (min)	52 (34–69)	48 (38–70)	46 (38–71)
Lignocaine consumption (mg)	340 (300–420)	320 (300–400)	340 (300–420)

Table 2 Incidence of side-effects related to epidural morphine and the proportion of parturients requiring rescue antiemetic. Data are numbers of patients (%) with symptoms in a 24 h observation period. *P<0.05, **P<0.01 compared with saline group, using a 3×3 χ^2 test followed by a 2×2 χ^2 test

Side-effect	Group		
	Dexamethasone (n=38)	**Droperidol (n=38)**	**Saline (n=37)**
Nausea/vomiting			
Nausea	4 (11)	5 (13)	11 (30)
Vomiting	3 (8)	3 (8)	8 (22)
Total	7 (18)**	8 (21)*	19 (51)
Patients requiring rescue antiemetic	4 (11)*	5 (13)*	15 (41)
Pruritus			
Pruritus but only in a small area of the body	12 (32)	12 (32)	12 (32)
Generalized pruritus	5 (13)	4 (11)	5 (14)
Total	17 (45)	16 (42)	17 (46)

parturients who required rescue antiemetic (metoclopramide) were 11% in the dexamethasone group and 13% in the droperidol group, in comparison with 41% in the saline group (P<0.05) (Table 2).

The incidence of pruritus was similar among groups (45% in the dexamethasone group, 42% in the droperidol group and 46% in the saline group) (Table 2). Six parturients (16%) in the droperidol group reported restlessness. No parturient in the other two groups reported this (P<0.05). No parturient reported wound infection or delayed wound healing.

Discussion

In the present study we found that the total incidence of nausea and vomiting after epidural morphine was 51% when no antiemetic was given prophylactically. After pretreatment with either dexamethasone or droperidol, the total incidence of nausea and vomiting was significantly reduced. Both dexamethasone and droperidol were effective in preventing epidural morphine-related nausea and vomiting in parturients undergoing Caesarean section. However, those who received droperidol reported a higher incidence of restlessness.

Dexamethasone is effective in preventing nausea and vomiting associated with chemotherapy.[12 13] Recently, dexamethasone has also been reported to be effective in preventing PONV in patients undergoing tonsillectomy, thyroidectomy, cholecystectomy and hysterectomy.[17 20–23] In a previous study, we also found that dexamethasone is effective in preventing nausea and vomiting associated with epidural morphine in patients undergoing abdominal hysterectomy.[11] Because of these data, we hypothesized that dexamethasone might also be effective in preventing nausea and vomiting after epidural morphine for analgesia after Caesarean section.

The exact mechanism by which dexamethasone, a glucocorticoid, exerts an antiemetic action after epidural morphine is not known. Glucocorticoids have been shown to have various effects on the central nervous system; they regulate transmitter levels, receptor densities and neurone configuration.[25 26] Numerous glucocorticoid receptors are found in the nucleus of the solitary tract, the nucleus of raphe and the area postrema.[26 27] These nuclei are well known to have significant neuronal activity in the regulation of nausea and vomiting.[10 19] Dexamethasone may exert its antiemetic action through these nuclei.

We also found that dexamethasone did not influence the efficacy of epidural morphine-related analgesia. Parturients in the three groups required similar amounts of rescue analgesic and reported similar intensities of postoperative pain. Also, i.v. dexamethasone did not influence the occurrence of pruritus related to epidural morphine for post-Caesarean section analgesia.

A wide dose range of dexamethasone (8–32 mg) has been used in the management of PONV and emesis associated with chemotherapy.[12–15 17–23] A dose of 8–10 mg has been used most frequently in the prevention of PONV.[17 20 23] For example, an 8 mg dose of dexamethasone was effective in the prevention of nausea and vomiting after epidural morphine in patients undergoing abdominal hysterectomy.[11] Therefore an 8 mg dose was chosen in this study. However, dose–response studies are needed to determine the optimal dose of dexamethasone.

The long-term administration of corticosteroids is associated with side-effects, such as increased risk of infection, delayed wound healing, glucose intolerance and adrenal suppression. However, we were unable to find a report of these adverse effects related to a single dose of dexamethasone, and delayed wound healing or wound infection did not occur in our study. Although a single dose of dexamethasone is considered safe, further study is indicated.

Droperidol also has a potent antiemetic effect.[28 29] Previous studies have demonstrated that its antiemetic effect is equal to that of ondansetron and superior to that of metoclopramide in preventing PONV.[28 29] The recommended dose for this purpose is 1.25 mg.[29] In our study, we also found that droperidol 1.25 mg is effective in preventing nausea and vomiting related to epidural morphine for post-Caesarean section analgesia. However, droperidol is not devoid of side-effects. Restlessness, a common droperidol-related side-effect, was found in 16% parturients who received droperidol 1.25 mg in our study. Although this side-effect was relieved by the i.m. diphenhydramine, it nevertheless produced mental distress in our patients. Because dexamethasone demonstrated a significant antiemetic effect without evident adverse effects, it may be a valuable treatment for the prophylaxis of epidural morphine-related nausea and vomiting in parturients receiving Caesarean section.

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