Risk Factors of Vomiting Among Females on Patient-controlled Epidural Analgesia

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Background: Postoperative pain and postoperative vomiting (POV) are both sources of distress in the postoperative period. Patient-controlled epidural analgesia (PCEA) is used in patients undergoing lower extremity surgery to improve postoperative quality but is accompanied by a certain incidence of vomiting. We wanted to determine the risk factors of POV in patients using PCEA with the aim of improving the quality of the postoperative period.

Methods: We conducted a retrospective study to analyze the risk factors among patients using PCEA after lower-limb surgery under regional anesthesia. A total of 195 patients (91 males, 104 females) were enrolled. They were categorized into 2 groups: vomiting and non-vomiting. We found that female gender predominated in the vomiting group. Hence, we analyzed the female subgroup in order to find the risk factors of vomiting in the female PCEA population.

Results: Female gender was the most significant factor related to vomiting (crude OR, 11.55; 95% CI, 4.88–27.33). From analysis of the female subgroup, puncture site (OR, 4.07; 95% CI, 1.41–11.79), catheter length in the epidural space (OR, 0.28; 95% CI, 0.16–0.50) and patient's height (OR, 1.07; 95% CI, 1.00–1.14) were also factors for vomiting, i.e. higher epidural catheter puncture site, shorter length in the epidural space, and greater height caused a higher incidence of POV.

Conclusion: The most important risk factor for POV in patients using PCEA was female gender. Among the female subgroup, the risk factors for POV included higher epidural catheter puncture site, shorter length in the epidural space and greater body height. [*J Chin Med Assoc* 2009;72(4):183–187]

Key Words: epidural analgesia, epidural catheter, logistic regression model, patient-controlled analgesia, postoperative vomiting

Introduction

Postoperative vomiting (POV) is a source of distress for patients after anesthesia and surgery and may delay discharge from, or cause readmission to, hospital.[1,2] Risk factors associated with POV include female gender, nonsmoking status, history of POV or motion sickness, extended duration of anesthesia, postoperative opioid use, and age.[3] Compared with general anesthesia, regional anesthesia causes a lower incidence of POV for the avoidance usage of volatile anesthetics or neostigmine.[3–6] From our previous study, we found that female gender is the only risk factor for POV in patients undergoing lower-limb surgery with postoperative patient-controlled epidural analgesia (PCEA).[7] The incidence rate of POV in our previous study was < 10%. This rate seems fairly low in comparison with that of other studies.[8–11] Underestimation of the incidence of POV was possible. Hence, we conducted this study to investigate the potential risk factors associated with POV during the course of PCEA. Subgroup analysis for female gender was also performed to evaluate the effect of these factors on POV in this higher risk group.

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Methods

This study was conducted at Taipei Veterans General Hospital, a tertiary medical center in Taiwan. Ethical approval was obtained from our Institutional Review Board (VGHIRB No. 96-10-07A). We collected data on orthopedic surgical patients consenting to epidural analgesia from January to March 2007. Patients who underwent operations involving the lower extremities under combined spinal-epidural anesthesia with postoperative PCEA were enrolled in the analysis. Patients with missing demographic data or malfunctioning epidural catheters were excluded. Epidural catheters were placed when performing spinal anesthesia before operation with paramedian approach in an intervertebral space corresponding to the dermatome level of the surgical incision, with the patient in the lateral decubitus position. After local infiltration with 2% lidocaine, spinal anesthesia was performed and followed by epidural catheter placement. An 18-gauge Tuohy needle and 20-gauge epidural catheter were employed. Epidural space was identified with the loss-of-resistance technique, and the epidural catheter was placed 5–8 cm into the epidural space according to the preference of the anesthesiologist. The catheter entry point was dressed with transparent adhesive dressing for inspection of catheter dislodgment or signs of local infection. All epidural catheters were confirmed not to have kinking or malposition. If the epidural catheter had an obstruction, or if intrathecal or intravascular migration was noted, the catheter was removed and the patient was excluded from this study. Regional anesthesia was performed with intrathecal hyperbaric 0.5% bupivacaine 12–15 mg and epidural top-up dose of 6–10 mL bupivacaine (0.5%), with fentanyl (5 μg/mL) given if the sensory block regressed before the end of operation. Otherwise, epidural loading dose with 6–10 mL bupivacaine (0.25%) and fentanyl (5 μg/mL) was administered at the end of operation.

As soon as patients arrived in the postanesthesia care unit, they were educated on how to use the patient-controlled analgesia pump (Aim® Plus System; Abbott Laboratories, North Chicago, IL, USA), and the background infusion was started. The infused drug comprised local anesthetic (0.1% bupivacaine) and opioid (1 μg/mL fentanyl). Initial PCEA settings were a background infusion of 4 mL/hr with a PCEA bolus of 2 mL and lockout interval of 20–30 minutes. Pain intensity was assessed using an 11-point verbal analog scale (VAS) (0 = no pain to 10 = worst pain imaginable). Inadequate resting analgesia (VAS ≥ 4) was secured with a 5-mL top-up dose of the infusion mixture, and the background infusion dose was adjusted to 5–6 mL/hr.

Table 1. Definitions of factors

Factor	Definition
Length	Epidural catheter length in the epidural space
Height	Patient body height
Weight	Patient body weight
Bolus dose	The first loading dose of patient-controlled analgesia
Puncture site	The epidural catheter insertion site. Epidural puncture site above L2/L3 (above L2/3 = 1; L3/4, L4/5 = 0)

All patients were visited at least once a day by the staff of the acute pain service (APS) and whenever clinically needed. Any complaint of numbness, nausea, vomiting, pruritus or other adverse effects related to PCEA was treated with 1–2 mL/hr decrease in continuous dose based on the clinical severity, and it was recorded in the PCEA recording charts. The definitions of factors used in this article are shown in Table 1.

Recruited patients were categorized into the vomiting or non-vomiting group according to their response to PCEA. Patients who experienced vomiting were placed in the vomiting group and patients who did not vomit during the PCEA period were placed in the non-vomiting group.

Continuous data are presented as mean ± standard deviation (SD), and categorical data are expressed as number with percentage. Independent t test or χ^2 test was used to compare patients' characteristics and variables related to PCEA usage of the 2 groups. Any p value < 0.05 was considered statistically significant. Logistic regression analyses were used for odds ratio (OR) estimation. After univariate analysis, forward stepping of variables was performed with pre-assigned p values equal to 0.05 for controlling the stepping retention. The OR estimates are exhibited with their 95% confidence intervals (CI). Subgroup analysis was also conducted to evaluate the risk factors for vomiting in females. Receiver operating characteristic (ROC) curve was used to assess the fit of the model. All statistical analyses were carried out using SPSS version 15.0 (SPSS Inc., Chicago, IL, USA) for Windows.

Results

A total of 195 patients (91 men, 104 women) were enrolled in the study. The demographic data and variables related to PCEA usage were compared between the vomiting and non-vomiting groups (Table 2). The incidence of POV in our study was 30% (51 females,

Table 2. Demographic data of the enrolled patients*

	Non-vomiting ($n=137$)	Vomiting ($n=58$)	p	Total ($n=195$)
Age (yr)	69.5 ± 12.9	69.6 ± 10.9	0.954	69.6 ± 12.3
Length (cm)†	6.8 ± 0.9	6.3 ± 0.8	< 0.001§	6.7 ± 0.9
Height (cm)	159.6 ± 10	154.8 ± 6.5	< 0.001§	158.2 ± 9.3
Weight (kg)	66.3 ± 11.9	62.9 ± 11.2	0.06	65.3 ± 11.7
BMI (kg/m^2)	26 ± 4.2	26.2 ± 4.1	0.84	26.1 ± 4.1
Bolus dose (mL)	2 ± 0.3	2 ± 0.2	0.298	2 ± 0.3
Sex (female)	53 (38.7)	51 (87.9)	< 0.001§	104 (53.3)
Total knee replacement	92 (67.2)	41 (70.7)	0.628	133 (68.2)
Puncture site‡	109 (79.6)	49 (84.5)	0.423	158 (81.0)

**Data presented as mean ± standard deviation or n (%); †catheter length indwelling in the epidural space; ‡epidural catheter insertion site above the level of the 3rd lumbar vertebra; §total knee replacement, $p < 0.05$. BMI = body mass index.*

Table 3. Crude and adjusted OR of potential risk factors related to PCEA-induced vomiting

	Crude OR	95% CI		p (univariate)	Adjusted OR	95% CI		p (multivariate)
		Lower	Upper			Lower	Upper	
Sex (female)	11.55	4.88	27.33	< 0.001*	66.37	14.93	294.97	< 0.001*
Age (yr)	1.00	0.98	1.03	0.953				
Total knee replacement	1.18	0.60	2.30	0.628				
Site	1.40	0.61	3.19	0.424	4.07	1.41	11.79	0.01*
Length (cm)	0.54	0.38	0.77	0.001*	0.28	0.16	0.50	< 0.001*
Height (cm)	0.94	0.91	0.98	0.001*	1.07	1.00	1.14	0.045*
Weight (kg)	0.97	0.95	1.00	0.062				
Bolus dose (mL)	0.57	0.19	1.67	0.302				
BMI (kg/m^2)	1.01	0.94	1.09	0.839				

**$p < 0.05$. OR = odds ratio; PCEA = patient-controlled epidural analgesia; CI = confidence interval; BMI = body mass index.*

7 males). The length of the epidural catheter, patient height and sex distribution were significantly different between the vomiting and non-vomiting groups.

Table 3 shows the crude and adjusted ORs of some potential risk factors related to vomiting induced by PCEA. Univariate analyses showed that female sex, catheter length in the epidural space, and patient height and weight were associated with vomiting during the course of PCEA. Female sex was the most significant risk factor related to vomiting (crude OR, 11.55; 95% CI, 4.88–27.33). In contrast, longer catheter length in the epidural space, and patient body height and weight played protective roles in POV. The crude OR of catheter length in the epidural space was 0.54 (95% CI, 0.38–0.77). The crude OR of body height and weight were 0.94 and 0.97, respectively. Factors related to PCEA dosage, like bolus dose, were not associated with increased risk of vomiting. Other factors did not have statistically significant influence on vomiting.

The results of adjusted OR of significant factors after forward model selection are also presented in Table 3. Female sex remained the most significant risk factor related to PCEA-induced vomiting. The adjusted OR of female sex increased to 66.37 (95% CI, 14.93–294.97). Other risk factors after adjustment included higher epidural puncture site (intervertebral space between L2 and L3 *vs.* other lower intervertebral space: OR, 4.07; 95% CI, 1.41–11.79) and taller body height (OR, 1.07; 95% CI, 1.00–1.14). On the contrary, longer catheter length in the epidural space exerted a protective effect (OR, 0.28; 95% CI, 0.16–0.50).

Subgroup analysis results between vomiting and non-vomiting for female patients are displayed in Table 4. The epidural catheter length, height and total knee replacement were significantly different between the 2 groups. Figure 1 illustrates the ROC curve of the final selected model. The area under the curve (AUC) was about 0.87 (95% CI, 0.81–0.93), indicating that the selected model fit the observed data well. Table 5 presents the results of female subgroup analysis. There were 3 factors related to POV in females, including higher puncture site (OR, 9.52; 95% CI, 1.91–47.51), longer catheter length in the epidural space (OR, 0.08; 95% CI, 0.02–0.30), and taller patient height (OR, 1.15; 95% CI, 1.05–1.25).

Table 4. Subgroup analysis for female sex*

	Non-vomiting ($n=53$)	Vomiting ($n=51$)	p
Age (yr)	70.2 ± 8.4	67.7 ± 10.0	0.169
Length (cm)†	7.0 ± 0.6	6.4 ± 0.7	< 0.001§
Height (cm)	150.5 ± 5.3	154.0 ± 6.2	0.003§
Weight (kg)	61.1 ± 9.1	63.2 ± 11.4	0.303
BMI (kg/m^2)	27.0 ± 4.1	26.6 ± 4.1	0.596
Bolus dose (mL)	2.0 ± 0.2	2.0 ± 0.2	0.845
Total knee replacement	46 (86.8)	36 (70.6)	0.043§
Puncture site‡	37 (69.8)	42 (82.4)	0.135

**Data presented as mean ± standard deviation or n (%); †catheter length indwelling in the epidural space; ‡epidural catheter insertion site above the level of the 3rd lumbar vertebra; §p < 0.05. BMI = body mass index.*

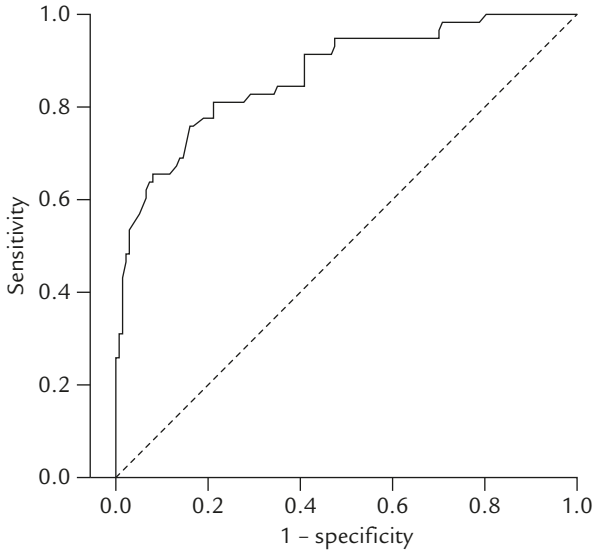

Figure 1. Receiver operating characteristic curve of the final selected model. The area under the curve is about 0.87, with 95% confidence intervals of 0.81–0.93. Diagonal segments are produced by ties.

Discussion

From the analyses, we found that the risk factor for vomiting in female patients using PCEA was higher epidural catheter puncture site. Longer threaded epidural catheter exerted a protective effect. The overall incidence of POV in this study was 30%. The incidence of POV in our last study was 9.7%.[7] It seemed that distinct investigators caused underestimation of the incidence of POV in our previous study.

The analgesia mechanism of fentanyl in the epidural space is not clearly understood. It is presumed that the lipophilic opioids injected into the epidural space work by spinal effect and systemic uptake.[12–17]

Table 5. Result of female subgroup analysis*

Factor	Adjusted OR	95% CI		p (multivariate)
		Lower	Upper	
Site	9.52	1.91	47.51	0.006†
Length (cm)	0.08	0.02	0.30	< 0.001†
Height (cm)	1.15	1.05	1.25	0.002†

**There were 3 factors related to PCEA-induced vomiting in females, including puncture site, catheter length, and patient height; †p < 0.05. OR = odds ratio; CI = confidence interval; PCEA = patient-controlled epidural analgesia.*

Compared with hydrophilic opioids such as morphine, the advantage of fentanyl in the epidural space is characterized by its lipophilic nature, which exerts segmental effect other than rostral spread to cause side effects, such as vomiting.[4] The side effect of vomiting from the use of fentanyl in the epidural space is believed to be induced by systemic absorption reaching the chemoreceptor trigger zone.

The ideal epidural catheter location is regarded to be congruent to the incisional dermatome to offer better analgesia and fewer side effects. In lower-extremity surgery, the ideal congruent epidural catheter location is L1–L4. If the indwelling epidural catheter lengths are all 5 cm, the higher insertion site theoretically means a higher tip position. Our PCEA analgesic agent included local anesthetic agent (0.1% bupivacaine) and opioid (1 μg/mL fentanyl). Opioid is thought to be the contributor to POV. But the mechanism of vomiting is complex, and vagus nerve also plays a role in provoking vomiting.[18] The epidural local anesthetic's precise location of action is not clearly understood; the potential sites include the spinal nerve roots, dorsal root ganglion and the spinal cord itself.[14] The epidural local anesthetics may cause sympatholytic effect and consequently unopposed parasympathetic tone. Vagal tone dominance may increase the incidence of POV.[4,18] The higher the epidural catheter tip, the more extended the range of sympathetic blockage, which causes POV. Since drug spread in the epidural space is not predictable,[19] the larger volume did not make the higher level blockage. So the bolus dose is not selected into the final regression model.

In the univariate analysis, the crude OR for patient height was 0.94 (95% CI, 0.91–0.98). It seemed that patients of shorter stature had a higher possibility of PCEA-induced vomiting. But after multivariate selection, the adjusted OR became 1.07 (95% CI, 1.00–1.14). On average, the body height of females is generally shorter than that for males. After excluding the effect of sex interference by multivariate logistic regression, we found that the taller patients had a higher

incidence of vomiting. On the other hand, both crude and adjusted ORs of height were very close to 1. Either our data were insufficient to provide a definite conclusion or patient height (compared with other factors) only played a minor role in PCEA-induced vomiting in the final regression model.

Why was the longer epidural catheter length a protective factor? We know that longer epidural catheter length insertion increases the risk of intravenous insertion, intrathecal migration, knotting or unilateral sensory analgesia.[20] From our literature review, there is no study on the relation between epidural catheter length and the incidence of POV. This is a remarkable finding, but the exact protective mechanism is not clear. The relationship between the incidence of POV in PCEA and epidural catheter length awaits further investigation.

In conclusion, the incidence of vomiting in patients with PCEA was 30% in this study. The predominant risk factor is female sex. Among the female population, we found that taller stature and higher epidural catheter puncture level were risk factors for vomiting; longer threaded catheter length was a protective factor for POV in patients using PCEA. The relationship between catheter length and incidence of POV needs further study. In daily practice, to reduce the incidence of POV, we may choose a lower puncture site for epidural catheter insertion, especially in the taller female population.

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