INTRODUCTION

Postoperative nausea and vomiting (PONV) is one of the most common and distressing complications after surgery. An identification of risk factors associated with PONV would make it easier to select specific patients for effective antiemetic therapy. We designed a case-controlled study to identify the risk factors for PONV in 5,272 surgical patients. At postoperative 2 and 24 hr, patients were visited and interviewed on the presence and severity of PONV. Thirty nine percent of patients experienced one or more episodes of nausea or vomiting. Five risk factors were highly predictive of PONV: 1) female, 2) history of previous PONV or motion sickness, 3) duration of anesthesia more than 1 hour, 4) non-smoking status, and 5) use of opioid in the form of patient controlled analgesia (PCA), in the order of relevance. The formula to calculate the probability of PONV using the multiple regression analysis was as follows: \( P = \frac{1}{1 + e^{-Z}} \), where \( Z = -1.885 + 0.894 \times \text{gender} + 0.661 \times \text{history} + 0.584 \times \text{duration} + 0.196 \times \text{smoking} + 0.186 \times \text{PCA-based opioid} \). Key Words: Models, Statistical; Postoperative Nausea and Vomiting; Risk Factors

A Korean Predictive Model for Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) is one of the most common and distressing complications after surgery. An identification of risk factors associated with PONV would make it easier to select specific patients for effective antiemetic therapy. We designed a case-controlled study to identify the risk factors for PONV in 5,272 surgical patients. At postoperative 2 and 24 hr, patients were visited and interviewed on the presence and severity of PONV. Thirty nine percent of patients experienced one or more episodes of nausea or vomiting. Five risk factors were highly predictive of PONV: 1) female, 2) history of previous PONV or motion sickness, 3) duration of anesthesia more than 1 hour, 4) non-smoking status, and 5) use of opioid in the form of patient controlled analgesia (PCA), in the order of relevance. The formula to calculate the probability of PONV using the multiple regression analysis was as follows: \( P = \frac{1}{1 + e^{-Z}} \), where \( Z = -1.885 + 0.894 \times \text{gender} + 0.661 \times \text{history} + 0.584 \times \text{duration} + 0.196 \times \text{smoking} + 0.186 \times \text{PCA-based opioid} \). Key Words: Models, Statistical; Postoperative Nausea and Vomiting; Risk Factors

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MATERIALS AND METHODS

With approval of the Institutional Review Board, we enrolled 5,272 inpatients over 15 yr old from 20 April to 10 August 2004 in this case-controlled study. Patients who were transferred to intensive care unit, discharged on the same day, received local anesthesia or had communication difficulties were excluded.

Perioperative anesthetic techniques whether general or regional anesthesia and anesthetic drugs administered to the patients were at the discretion of the anesthesiologists.

At two hours after the surgery in the PACU, the presence and severity of PONV, history of previous PONV and motion sickness, and smoking status were interviewed by one of the researchers. Additionally, at 24 hr after the surgery, the presence and severity of PONV and post-operative opioid use with patient-controlled analgesia (PCA) device were recorded at ward by one of our investigators. PCA regimens varied according to the type of surgeries but all included opioids such as morphine and fentanyl in their components. Preoperative patient characteristics and intra-operative variables were recorded on specifically designed, standardized study forms. Each patient was regarded as having PONV when he or she experienced any nausea and/or vomiting within the first 24 post-operative periods.

Descriptive statistics on characteristics of patients, surgery, and anesthesia were denoted in characteristics and their frequencies. For categorical variables, the chi-square analysis was performed to estimate the statistical differences. For continuous variables, the Student t test was used to compare their mean values between PONV and non-PONV groups.

To identify independent predictors for PONV, we used a multiple logistic regression analysis using a forward selection procedure (p ≤ 0.000 to enter). In this model, the estimated probability of PONV, denoted by P, depends on the score Z according to the formula

\[ P = \frac{1}{1 + e^{-Z}} \]

in which, \( Z = b_0 + b_1z_1 + \ldots + b_kz_k + e \) is a weighted sum of the values \( z_1, \ldots , z_k \) of \( e \) risk factor or predictor, coded as 1 if present and 0 if absent, with \( b_0, \ldots , b_k \) as the weight or estimated regression coefficient, and each described as the log odds-ratio associated with the corresponding factor (so that the corresponding odds ratio is obtained from OR = exp(b) for factor j). The intercept \( b_0 \) means the baseline log odds of PONV, that is, \( P_c = 1/1 + e^{b_0} \) is the estimated baseline risk of PONV in a patient without any risk factors.

RESULTS

Overall, thirty nine percent of patients (2,063 out of 5,272 patients) experienced PONV either in the PACU or at ward. The incidence of PONV in the PACU was higher than at ward (27% vs. 21%, p ≤ 0.001). Among 2,063 patients with PONV, 946 patients (42%) in the PACU only, 625 patients (30%) at ward (27% vs. 21%, p < 0.001) (Table 1).

As less relevant risk factors of PONV, the use of propofol was related to lower occurrence of PONV in the PACU than inhalational agents. Low body mass index (BMI) (<25) was associated with PONV than high BMI (≥25). The American Society of Anesthesiologists (ASA) physical status, the use of N2O, and the use of opioids in the operating room or in the PACU were not significant predictors of PONV.

Table 1. Incidences of PONV

|                | PACU Ward | PACU+Ward |
|----------------|-----------|-----------|
| PONV (−)       | 3,834 (72.72) | 4,155 (78.81) | 3,209 (60.87) |
| PONV (+)       | 1,436 (27.28) | 1,117 (21.19) | 2,063 (39.13) |
| Nausea         | 1,160 (22.00) | 829 (15.73) | 1,526 (28.95) |
| Retching       | 112 (2.13) | 29 (0.55) | 132 (2.50) |
| Vomiting       | 166 (3.15) | 259 (4.91) | 405 (7.68) |

Values are numbers of patients (%); PACU, post-anesthesia care unit.

Table 2. Risk factors for PONV

| Number | % | OR  | CI  | p   |
|--------|---|-----|-----|-----|
| Gender |   |     |     |     |
| Male   | 2,344 | 26 | 2.9 | 2.61-3.31 | 0.000 |
| Female | 2,928 | 50 |     |     |     |
| History|   |     |     |     |
| No     | 3,964 | 34 | 2.4 | 2.11-2.73 | 0.000 |
| Yes    | 1,308 | 55 |     |     |     |
| Non-smoking |   |     |     |     |
| No     | 1,055 | 27 | 2.0 | 1.75-2.36 | 0.000 |
| Yes    | 4,217 | 42 |     |     |     |
| OP duration |   |     |     |     |
| ≤ 1 hr | 645 | 27 | 1.9 | 1.55-2.23 | 0.000 |
| > 1 hr | 4,627 | 40 |     |     |     |
| PCA use |   |     |     |     |
| No     | 3,260 | 37 | 1.28 | 1.14-1.43 | 0.000 |
| Yes    | 2,012 | 43 |     |     |     |
| Anesthetic agent |   |     |     |     |
| Volatile | 5,317 | 27 | 1.96 | 1.21-3.25 | 0.002 |
| Propofol | 135 | 16 |     |     |     |
| BMI (kg/m²) |   |     |     |     |
| < 25  | 3,252 | 40 | 1.18 | 1.03-1.33 | 0.004 |
| ≥ 25  | 2,000 | 36 |     |     |     |
| ASA class |   |     |     |     |
| I     | 3,309 | 40 | 0.63 |     |     |
| Others | 1,963 | 37 |     |     |     |
| N2O   |   |     |     |     |
| No     | 2,059 | 40 | 0.12 |     |     |
| Yes    | 3,213 | 38 |     |     |     |
| PCA mode |   |     |     |     |
| IV     | 1,840 | 39 | 0.77 |     |     |
| Epidural | 182 | 41 |     |     |     |
| Intra-OP opioid |   |     |     |     |
| No     | 3,139 | 39 | 0.70 |     |     |
| Yes    | 2,135 | 39 |     |     |     |
| PACU opioid |   |     |     |     |
| No     | 868  | 39 | 0.99 |     |     |
| Yes    | 4,404 | 39 |     |     |     |

Number, number of patients; OR, odds ratio; CI, confidence interval; History, history of PONV or motion sickness; OP, operation; PCA, patient-controlled analgesia; BMI, body mass index; N2O, use of N2O during anesthesia; PACU, post anesthesia care unit. (28%) newly at ward, and 492 patients (22%) had PONV at the two places together. Nausea was more frequently observed in the PACU, whereas the incidence of vomiting was higher at ward (p<0.001) (Table 1).

Using a multiple logistic regression analysis with a forward selection, we found that female, history of previous PONV or motion sickness, duration of anesthesia more than one hour, non-smoking status, and the use of PCA-based opioid were high risk factors of PONV in the order of relevance (Table 2).

As less relevant risk factors of PONV, the use of propofol was related to lower occurrence of PONV in the PACU than inhalational agents. Low body mass index (BMI) (<25) was associated with PONV than high BMI (≥25). The American Society of Anesthesiologists (ASA) physical status, the use of N2O, and the use of opioids in the operating room or in the PACU were not significant predictors of PONV. The
Values are number of patients (%). OPH, ophthalmic surgery.

| Procedure                  | PONV (-) | PONV (+) |
|----------------------------|----------|----------|
| Laparotomy (n=1,334)       | 840 (63) | 494 (37) |
| Laparoscopy (n=523)        | 293 (56) | 230 (44) |
| Orthopedic (n=603)         | 456 (58) | 336 (42) |
| Neurosurgery (n=163)       | 126 (59) | 88 (41)  |
| Vascular (n=47)            | 51 (83)  | 11 (17)  |
| Maxillofacial (n=56)       | 34 (46)  | 40 (54)  |
| Gynecology (n=555)         | 362 (50) | 368 (50) |
| Urology (n=236)            | 225 (72) | 87 (28)  |
| Plastic (n=128)            | 92 (55)  | 76 (45)  |
| Otolaryngology (n=511)     | 424 (63) | 249 (37) |
| Abdominal (n=568)          | 460 (62) | 288 (38) |
| Sigmoidectomy (n=326)      | 311 (72) | 119 (28) |
| Major breast (n=244)       | 200 (62) | 121 (38) |
| Thyroid (n=168)            | 100 (45) | 121 (55) |
| Thoracic (n=307)           | 287 (71) | 117 (29) |
| OPH (n=75)                 | 54 (55)  | 45 (45)  |
| Other surgery (n=18)       | 20 (83)  | 4 (17)   |

Table 3. Distribution of the patients with PONV according to type of surgery

mode of PCA whether intravenous or epidural, did not show any difference in the frequency of PONV (Table 2). The type of anesthesia (general vs. regional) was not associated with the risk of PONV (39% vs. 41%). There was no statistical correlation between age and PONV (the incidences of PONV were 30, 42, 43, 40, 36, 37, 42%, and 36% at every 10 yr interval until 80 yr old).

There was a wide variation in the incidence of PONV according to the type of surgery. The frequency of PONV was significantly higher in the patients undergoing laparoscopic procedure than laparotomy (44% vs. 37%, OR 1.33, p=0.007). Certain type of operations such as maxillofacial, gynecologic, and thyroid operations showed high incidence of PONV (>50%) (Table 3).

Based on the above results, we developed a predictive model to calculate the probability of PONV:

\[ P = \frac{1}{1 + e^{-Z}} \]

where \( Z = -1.885 + 0.894 \text{ (gender)} + 0.661 \text{ (history)} + 0.584 \text{ (duration of anesthesia)} + 0.196 \text{ (smoking status)} + 0.186 \text{ (use of PCA-based opioid)} \).

\{ \text{gender: female}=1, \text{male}=0; \text{history of previous PONV or motion sickness: yes}=1, \text{no}=0; \text{duration of anesthesia: more than 1 hr}=1, \text{less than or 1 hr}=0; \text{smoking status: no}=1, \text{yes}=0; \text{use of PCA-based opioid: yes}=1, \text{no}=0 \} \) (Table 4).

**DISCUSSION**

This study was conducted in a large population of 5,272 patients undergoing various operations, and 39% of patients experienced PONV either in the PACU or at ward. We analyzed the characteristics of each patient and the type of operations and anesthesia to reveal the relationship of every aspect of those factors with PONV.

Overall incidence of PONV was higher in the PACU than at ward. However, the incidence of vomiting was higher at ward (Table 1). The influence of remaining anesthetic agents might have affected the occurrence of nausea in the PACU and the movement or ambulation of patients at ward might have contributed to the occurrence of vomiting. Contrary to our study, both nausea and vomiting were more frequent at ward than in the PACU in other studies (2, 7, 12).

In this study, gender, history of previous PONV or motion sickness, duration of anesthesia, smoking status, and use of PCA-based opioid were identified as independent predictors of PONV. The correlation of female gender has been well demonstrated and appeared as the most important predictor of PONV (2, 7, 12-16). Likewise, female gender was the most influential risk factor for PONV in our study with an odds ratio of 2.9. The gender difference was not noted in the preadolescent age group or in patients beyond the 8th decade of life, suggesting that variations in serum gonadotropin levels might be a contributing factor in the higher incidence of emesis in women (12, 17).

Another predictor of PONV was history of previous PONV or motion sickness, and it was the second strongest predictor of PONV in this study (odds ratio of 2.4). Tramer et al. (3) have outlined a decision tree for PONV prophylaxis in adults that a positive history of PONV is sufficient to justify the use of prophylactic antiemetics.

The duration of anesthesia was also a predictor of PONV, and the odds ratio was 1.9 for the anesthesia time longer than 1 hr. Pre-medication, volatile anesthetics with nitrous oxide, prolonged fasting, and pain may contribute to the increased incidence of PONV in longer procedures (12, 17).

Another predictor of PONV was smoking status. Non-smoking showed an odds ratio of 2.0 in this study. Chronic exposure to toxic gas (tobacco) may desensitize a patient’s reaction to anesthetic gas. As another possible etiology, one of chemicals within cigarette smoke may have anti-emetic effect (18). In addition, chronic consumption of cigarette induces enzyme cytochrome P450 in liver, and high P450 enzyme induction in smokers disposes anesthetic agents more quickly than in non-smoker resulting in less PONV (19).
The final major risk factor was the use of PCA-based opioid. Opioids are well known emetogenic agents and opioid-induced nausea and vomiting are frequently triggered by movement (17). In our study, the use of opioids in the operating room or in the PACU was not related to PONV, whereas postoperative use of opioids via PCA at ward was. The occurrence of PONV in patients at ward might be partly attributed by the patient’s movement. Sudden motion, changes in position, or even transport from the PACU to the ward can precipitate nausea and vomiting in patients who have received opioid compounds. Kamath et al. also demonstrated that 66% of PONV was related to movement (20).

Among other risk factors not included in this risk model, intravenous anesthesia using propofol has generally been known to have anti-emetic effect and reduce the incidence of PONV by half compared to inhalational anesthesia, though the antiemetic effect has been reported to be short-lived (21, 22). Likewise, in our study, the propofol’s antiemetic effect was noted only in the PACU (16% vs. 27%, p<0.002, OR 1.96).

High BMI is assumed to be related to higher occurrence of PONV. However, in our study, low BMI (<25) showed higher incidence of PONV (40% vs. 36%, p=0.004, OR 1.18). It might be due to the fact that female patients had lower BMI than male patients (BMI <25, M:F=965:1,940 versus BMI ≥25, M:F=1,024:1,304, p<0.001). Therefore, it could be presumed that gender has greater influence on PONV than BMI itself. Some other studies have reported that obesity has no effect or only minor effect on PONV (7, 12, 21).

The ASA physical status has been reported to be associated with the occurrence of PONV. Cohen et al. and others have demonstrated that a good physical condition as reflected by the low ASA physical status was one of the main risk factors of PONV (2, 23). However, our study showed that there was no significant correlation between the ASA physical status and the occurrence of PONV.

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