

# Incidence and Associated Factors of Postoperative Nausea and Vomiting in Patients Undergoing Craniotomy

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## บทคัดย่อ: อัตราการเกิดภาวะคลื่นไส้อาเจียนหลังผ่าตัดในผู้ป่วยผ่าตัดสมอง และปัจจัยที่เกี่ยวข้อง

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**ภูมิหลัง:** ภาวะคลื่นไส้อาเจียนหลังการผ่าตัด (postoperative nausea and vomiting, PONV) ในผู้ป่วยผ่าตัดสมองนั้นมีอุบัติการณ์ร้อยละ 10-74 โดยการผ่าตัดสมองเองนั้นก็เป็ปัจจัยเสี่ยงหนึ่งที่ทำให้เกิดการเกิดภาวะคลื่นไส้อาเจียนหลังการผ่าตัดสูงขึ้น การศึกษาเกี่ยวกับภาวะคลื่นไส้อาเจียนในผู้ป่วยผ่าตัดสมองส่วนใหญ่มักเป็นแบบย้อนไปข้างหลัง (retrospective) หรือเป็นการศึกษาที่มีขนาดเล็ก และมีการติดตามผู้ป่วยเป็นระยะเวลาสั้น การศึกษานี้จึงมีวัตถุประสงค์เพื่อศึกษาอัตราการเกิดและปัจจัยเสี่ยงของภาวะคลื่นไส้อาเจียนหลังผ่าตัดในผู้ป่วยผ่าตัดสมองที่โรงพยาบาลรามาธิบดี

**วิธีการ:** หลังจากได้รับการอนุมัติจากคณะกรรมการจริยธรรมว่าด้วยสิทธิมนุษยชนที่เกี่ยวข้องกับงานวิจัย งานวิจัยเชิงสังเกตแบบไปข้างหน้าจึงได้เริ่มทำการศึกษาในผู้ป่วยที่ได้รับการผ่าตัดสมอง 120 คน โดยผู้ป่วยมีอายุ 18-80 ปี และ ASA physical status I-IV ผู้วิจัยทำการเก็บข้อมูลภาวะคลื่นไส้อาเจียนหลังการผ่าตัด ในช่วง 1, 4, 24, 48, 72 ชั่วโมง ปัจจัยเสี่ยงทั้งหมดที่เกี่ยวข้องกับผู้ป่วย, การผ่าตัด และด้านวิสัญญีถูกนำมาวิเคราะห์

**ผล:** อัตราการเกิดภาวะคลื่นไส้อาเจียนหลังการผ่าตัดในผู้ป่วยผ่าตัดสมอง ที่ระยะเวลา 72 ชั่วโมงหลังผ่าตัด เท่ากับร้อยละ 35 ประวัติการเคยมีภาวะคลื่นไส้อาเจียนหลังการผ่าตัด หรือการเมาเหตุเคลื่อนไหว (motion sickness) (adjusted RR 46.611, 95% CI 4.077-532.924, p=0.002), การได้รับยากลุ่มโอปิออยด์ หลังผ่าตัด (adjusted RR 9.138, 95% CI 3.063-27.259, p<0.001), การได้รับเลือดระหว่างผ่าตัด (adjusted RR 4.886, 95% CI 1.601-14.907, p=0.005) และบริเวณในการผ่าตัดสมองที่ suboccipital (adjusted RR 8.134, 95% CI 2.052-32.239, p=0.003) นั้นเป็นปัจจัยเสี่ยงทำให้เกิดภาวะคลื่นไส้อาเจียนหลังการผ่าตัด อัตราการเกิดภาวะคลื่นไส้อาเจียนหลังการผ่าตัดลดลงในผู้ป่วยที่ได้รับยากลุ่มสเตียรอยด์ระหว่างการผ่าตัด (adjusted RR 0.274, 95% CI 0.08-0.936, p=0.039). **สรุป:** ภาวะคลื่นไส้อาเจียนหลังการผ่าตัด ในผู้ป่วยผ่าตัดสมองนั้นมีอุบัติการณ์ร้อยละ 35 ที่ระยะเวลา 72 ชั่วโมงหลังผ่าตัด ปัจจัยเสี่ยงที่เกี่ยวข้องกับภาวะคลื่นไส้อาเจียนหลังผ่าตัด คือ ผู้ป่วยที่มีประวัติ ภาวะคลื่นไส้อาเจียนหลังการผ่าตัดหรือการเมาเหตุเคลื่อนไหว การผ่าตัดสมอง suboccipital การให้เลือดและการได้รับยาแก้ปวดกลุ่มโอปิออยด์หลังผ่าตัด

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### Abstract

**Background:** Intracranial surgery is a risk factor of postoperative nausea and vomiting (PONV). Previous studies showed that the incidence rates of post craniotomy PONV varied from 10% to 74%. Most of them were retrospective, or observational studies. The objective of this study is to determine the incidence and risk factors of PONV after craniotomy at Ramathibodi Hospital. **Method:** After ethical approval from the Ethical Clearance Committee on Human Rights Related to Researches Involving Human Subjects, the prospective study was performed. Postoperative nausea and vomiting were prospectively assessed at 1, 4, 24, 48, and 72 hours after elective craniotomy in 120 patients, 18 to 80 years old with American Society of Anesthesiologists (ASA) classifications I to IV. Patients characteristic, surgical-related, and anesthetic-related risk factors of postoperative nausea and vomiting were recorded

and analyzed. **Result:** The overall incidence of PONV at 72 hours after elective craniotomy at Ramathibodi Hospital was 35%. The history of PONV / motion sickness (adjusted RR 46.611, 95% CI 4.077-532.924, p=0.002), postoperative opioid usage (adjusted RR 9.138, 95% CI 3.063-27.259, p<0.001), blood transfusion (adjusted RR 4.886, 95% CI 1.601-14.907, p=0.005) and suboccipital craniotomy (adjusted RR 8.134, 95% CI 2.052-32.239, p=0.003) are the risk factors of PONV. The incidence of PONV is significantly lower in the patients received steroid during the perioperative period (adjusted RR 0.274, 95% CI 0.08-0.936, p=0.039). **Conclusion:** The cumulative incidence of PONV after craniotomy, was 35% at 72 hour. The associated risk factors were previous history of PONV/ motion sickness, suboccipital surgery, blood transfusion, and postoperative opioids usage.

**Keywords:** Nausea, Vomiting, Craniotomy, Anesthesia

## Background

The most common complication in neurosurgery is postoperative nausea and vomiting (PONV)<sup>1</sup>. It causes patient discomfort and dissatisfaction. Moreover, it also causes fluid and electrolyte imbalance, aspiration of gastric contents, suture dehiscence, venous hypertension, bleeding<sup>2</sup>, poorer neurological recovery, prolongation of hospital stay, and increased healthcare resource usages.

In neurosurgical patients, PONV may increase intracranial pressure during vomiting which can potentially increase morbidity and mortality<sup>3</sup>. The previous studies, PONV incidence in post-craniotomy patients varies from 10% to 74%<sup>4</sup>. The overall incidence of postoperative nausea and vomiting (PONV) is around 30% and as great as 80% in high-risk patients<sup>5</sup>. The Intracranial procedure appeared to have an association with PONV. Other PONV risk factors related to neurosurgery such as sex, smoking status, a history of PONV, motion sickness and anesthesia related risk factors<sup>6</sup>, are still inconclusive.

The objective of this study is to examine the incidence of PONV in neurosurgery and perioperative predictive factors for PONV in the craniotomy surgery.

## Materials and Methods

The prospective study was performed after ethical approval from the Ethical Clearance Committee on Human Rights Related to Researches Involving Human Subjects, Ramathibodi Hospital. The study was conducted during January to July, 2015.

### Study participants

After endotracheal tube extubation of the elective craniotomy patients at the recovery room and ICU, well cooperation patients, aged 18-80 years old, American Society of Anesthesiologists (ASA) physical status I to IV, were included in this study. We excluded patients who performed emergency surgery, retained endotracheal tubes and were unable to communicate.

Sample size was calculated according to the study of Latz B et al.<sup>4</sup>. The incidence of PONV after craniotomy in their study was 47%. The power of 80% was expected for testing the odds ratio for Intra-operative administration of steroids [OR 4.48 (2.4-8.37)] and 10% of allowable error. The estimated sample size was 120 patients.

### Data collection

We collected patients' demographic and clinical characteristics, including sex, age, body mass index (BMI),

history of PONV/motion sickness and smoking status, diagnosis, and surgical procedure/site and also intraoperative data, duration of anesthesia, anesthetic agents, opioid dosage, steroid administration, amount of intravenous fluid, amount of blood loss, blood transfusion and PONV prophylaxis (dexamethasone or ondansetron). Nausea was defined as a subjectively unpleasant sensation associated with the awareness of the urge to vomit; retching was defined as labored, spasmodic, rhythmic contraction of the respiratory muscle without expulsion of gastric content from mouth.<sup>1</sup> The first episode timing of PONV, analgesic treatment and antiemetic treatment for either nausea or vomiting were recorded during the 3 days after the operation.

### Statistical analysis

Statistical analysis was performed by SPSS for Windows (versions 18.0, SPSS Inc.). Patient characteristics and other numerical data were analyzed using descriptive statistics. The t-test and chi-square were used for comparing mean and percentage between 2 groups. In order to identify risk factors associated with PONV, the univariate and multivariable were performed and variables with a P-value less than 0.1 were entered into a multiple logistic regression analysis, wherein P-values < 0.05 were considered significant.

## Results

120 participants were enrolled, 61.7% were female and patients with ASA classification II and III were 43.4% and 46.6% respectively. The mean age and BMI of patients were  $46 \pm 14$  years and  $24.5 \pm 5$  kg/m<sup>2</sup> respectively. All demographic data were shown in Table 1.

The overall incidence of PONV at 72 hours in patients undergoing craniotomy was 35% (42 patients). The PONV incidence of male: female was 33.3%: 66.7%. Most of the PONV was within the fourth hour after surgery, which was 69.0%, as shown in graph 1. Ninety nine patients (82.5%) were administered PONV prophylaxis with dexamethasone or ondansetron. The 32.3% (32 cases) of the patients who received PONV prophylaxis had PONV. The craniotomy patients with a history of PONV or motion sickness had a statistically significant ( $p < 0.001$ ) higher PONV than the others. The patients who smoked had a significant reduction in the incidence of PONV ( $p = 0.032$ ). Repeated PONV has a statistical significant in the patient with suboccipital craniotomy ( $p = 0.012$ ). The demographic data and patient characteristics between PONV and non PONV were shown in Table 2 and Table 3.

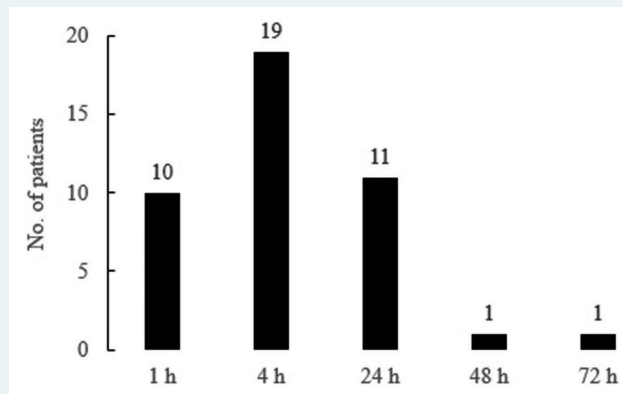
**Table 1** Demographic data (N=120)

Variable		Result
Gender N (%)	Male	46 (38.3%)
	Female	74 (61.7%)
Age (year) mean $\pm$ SD		46 $\pm$ 14
BMI (kg/m <sup>2</sup> ) mean $\pm$ SD		24.5 $\pm$ 5
ASA physical status N (%)	I	9 (7.5%)
	II	52 (43.4%)
	III	56 (46.6%)
	IV	3 (2.5%)

BMI = body mass index, ASA = American society of Anesthesiologists

The patients who had the history of PONV or motion sickness were the strongest predictor of PONV after craniotomy (adjusted RR 46.6, 95% confidence interval 4.0-532.9), following by the usage of postoperative opioids usage (9.1, 3.1-27.3),

suboccipital craniotomy (8.1, 2.1-32.2) and blood transfusion (4.9, 1.6-14.9). Perioperative steroid administration reduced the risk of PONV (0.3, 0.08-0.9). The univariate and multivariate analysis were shown in Table 4.

**Graph 1** The occurrence of first episode of PONV**Table 2** Comparison of demographic and patient characteristics between PONV and Non PONV groups

Variable	PONV group (n=42) N (%)	Non-PONV group (n=78) N (%)	P-value
Gender, n (%)			0.408
Male	14 (33.33%)	32 (41.03%)	
Female	28 (66.67%)	46 (58.97%)	
Age (year)	45.93 $\pm$ 16.23	47.56 $\pm$ 13.65	0.559
BMI (kg/m <sup>2</sup> )	25.05 $\pm$ 4.9	24.27 $\pm$ 5.35	0.43
ASA classification			0.605
I - II	20 (47.62%)	41 (52.56%)	
III - IV	22 (52.38%)	37 (47.44%)	
Smoking			0.032*
Smoker	1 (2.38%)	12 (15.38%)	
Non-smoker	41 (97.62%)	66 (84.62%)	
History of PONV/motion sickness			<0.001*
Yes	8 (19.05%)	-	
No	34 (80.95%)	78 (100%)	

PONV = postoperative nausea and vomiting, values presented as n (%), mean  $\pm$  SD, \*P<0.05

**Table 3** Type of surgery and anesthetic data

Variable	PONV group (n=42) N (%)	Non-PONV group (n=78) N (%)	P-value
Type of surgery			
Subdural	2 (4.76%)	1 (1.28%)	0.28
Aneurysm	-	1 (1.28%)	>0.999
AVM	3 (7.14%)	1 (1.28%)	0.123
Transphenoid	8 (19.05%)	22 (28.21%)	0.269
Frontal	12 (28.57%)	36 (46.15%)	0.061
Temporal	6 (14.29%)	7 (8.97%)	0.374
Occipital	-	3 (3.85%)	0.551
Suboccipital	11 (26.19%)	7 (8.97%)	0.012*
Anesthetic duration (min)			0.016*
> 240	29 (69.05%)	36 (46.15%)	
≤ 240	13 (30.95%)	42 (53.85%)	
Crystalloid (ml)	2869 ± 1236	2362 ± 1260	0.037*
Colloid			0.751
Yes	5 (11.9%)	7 (8.97%)	
Amount if yes (ml)	500 (500-3,200)	490 (100-2,000)	0.432
No	37 (88.1%)	71 (91.03%)	
Blood transfusion			0.037*
Yes	14 (33.33%)	13 (16.67%)	
Amount if yes (ml)	512 (200-1,030)	490 (100-2,000)	0.905
No	28 (66.67%)	65 (83.3%)	
Blood loss (ml)	350 (20-2,200)	275 (10-3,500)	0.203
Nitrous oxide			0.904
Yes	15 (35.71%)	27 (34.62%)	
No	27 (64.29%)	51 (65.38%)	
Inhalation agents			0.661
Desflurane	12 (28.57%)	25 (32.47%)	
Sevoflurane	30 (71.43%)	52 (67.53%)	
Intraoperative Fentanyl dose (mg)	250 (75-500)	200 (30-500)	0.002*
PONV Prophylaxis			0.182
Yes	32 (76.19%)	67 (85.9%)	
No	10 (23.81%)	11 (14.1%)	
Steroid administration			0.103
Yes	31 (73.8%)	67 (85.9%)	
No	11 (26.19%)	11 (14.1%)	
Postoperative opioids			<0.001*
Yes	32 (76.19%)	29 (37.18%)	
No	10 (23.81%)	49 (62.82%)	

AVM = arteriovenous malformation, values presented as n (%), mean ± SD, \*P<0.05

**Table 4** Univariate and multivariate analysis of factors associated with PONV.

Factors	Univariate analysis		Multivariate analysis	
	Unadjusted RR (CI)	P value	Adjusted RR (CI)	P value
Smoker	0.155 (0.021-1.15)	0.032*	NS	0.002*
History of PONV/motion sickness	3.093 (2.246-4.260)	<0.001*	46.611 (4.077-532.924)	
Suboccipital surgery	2.918 (1.222-6.967)	0.012*	8.134 (2.052-32.239)	0.003*
Anesthetic duration > 240 min	1.496 (1.093-2.047)	0.016*	NS	
Crystalloid	1 (1-1.001)	0.037*	NS	
Blood transfusion	2 (1.039-3.851)	0.037*	4.886 (1.601-14.907)	0.005*
Intraoperative Fentanyl dosage	1.006 (1.002-1.011)	0.002*	NS	
Post-op opioids usage	2.049 (1.467-2.863)	0.001*	9.138 (3.063-27.259)	<0.001*
Steroid administration	0.859 (0.703-1.051)	0.103	0.274 (0.08-0.936)	0.039*

\*P&lt;0.05

CI = Confidence interval

NS – non significant

## Discussion

PONV remains a significant problem in anesthesia practices despite a number of studies over decades. A PONV risk factor chart was developed by Apfel<sup>7</sup> identifying four main risks: female gender, non-smoker, history of PONV, and the use of perioperative opioids which lead to the general consensus to prophylactically treat those patients with moderate to high risk for PONV<sup>8</sup>. Data from previous studies regarding PONV predictors<sup>9</sup>, neurosurgery is generally believed to have an association with nausea/vomiting with incidence approximately more than 30%<sup>4</sup> because the surgery is performed in close proximity to the vomiting center in the midbrain (area postrema).

In this prospective study showed that PONV was 35% in 3 consecutively days after surgery. PONV occurred most in the first day (31%) after PACU period partly caused by residual anesthetic effects. Multivariate analysis identified these known risk factors : history of PONV/motion sickness, that had a strong correlation in this study (adjusted RR 46.6, 95% CI 4.07-532.9), and postoperative opioids usage, that increased nausea/vomiting risk nearly 10 times (adjusted RR 9.1, 95% CI 3.06-27.2). To reduce the risk of PONV, the authors suggest multimodal analgesia technique to reduce the opioids usage for controlling postoperative pain.

Dexamethasone is frequently used as a prophylactic antiemetic drug. In this study, the standard prophylaxis regimen (ondansetron 4-8 mg or dexamethasone 5 mg) did not reduce incidence of PONV. It failed to effectively prevent PONV. The higher dosage of dexamethasone or the combination of antiemetic drugs need further investigation.

Contrary to the previous studies from Latz<sup>4</sup>, female gender, smoking status, duration of anesthesia, type of inhalation, nitrous oxide, and intraoperative fentanyl dosage, did not demonstrate the risk factor of PONV in the study.

The type or location of craniotomy<sup>6</sup> is a controversial topic. This study showed that the site of the craniotomy was a positive correlation with PONV. Logistic regression revealed that suboccipital craniotomy was a high-risk surgery for PONV. This may be explained by the location of chemoreceptor trigger zone is in the infratentorial compartment. Surgical manipulation in this area may pose a risk of nausea/vomiting eventually.

Blood transfusion was identified as the risk factor in this study. The exact mechanism is unclear. The possible explanation might be that intravascular volume depletion or anemia was the cause of PONV.

There were several limitations in this study. Some of the patients received dexamethasone as a treatment for brain edema that was a PONV prophylaxis. The incidence of nausea and vomiting were not recorded separately. This research didn't investigate the pain score, oral intake, and hydration status. These factors might potentially influence PONV in postoperative period.

## Conclusion

The cumulative incidence of PONV after craniotomy, was 35% at 72 hour. The associated risk factors were previous history of PONV/motion sickness, suboccipital surgery, blood transfusion, and postoperative opioids usage. Multidisciplinary and multimodal interventions to prevent and treat PONV are necessary in patients undergoing craniotomy.

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