Postoperative Nausea and Vomiting After Minor Oral Surgery: A Retrospective Cohort Study

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Objective: This study aimed to determine whether PONV rates differed over time and to identify potential differences in PONV risk factors for oral surgery patients undergoing general inhalational anesthesia (IA) or propofol-based total intravenous anesthesia (TIVA).

Methods: This retrospective cohort study included patients between 16 and 85 years of age and who received intubated general anesthesia with either IA or TIVA for minor oral surgery between January 2021 and July 2022. Primary outcomes were PONV overall (onset at 0–24 hours), early (onset at 0–2 hours), and late (onset at 2–24 hours). Known PONV risk factors as identified from existing literature were included for analysis.

Results: Data were obtained from 188 patients. A total of 41 (21.8%) patients developed overall PONV, 35 patients (18.6%) had early PONV, and 14 patients (7.4%) had late PONV. Any PONV that occurred across 2 periods was categorized in each period. IA compared with TIVA had higher overall PONV (29.6% vs 13.3%; $P = .008$) and early PONV (25.5% vs 11.1%; $P = .034$). Female sex and increased Apfel scores were associated with increased overall, early, and late PONV. Per multivariate analysis, females were 2.5 to 6 times higher than males to have overall, early, and late PONV ($P < .05$), and IA was 3 times higher than TIVA to have overall and early, but not late, PONV ($P < .05$).

Conclusion: Our results suggested that the method of anesthesia may impact the incidence of overall and early PONV and that female sex and increase Apfel scores correlated with increased PONV through all times.

Key Words: Postoperative nausea and vomiting; Propofol; Total intravenous anesthesia; Inhalation anesthesia; Oral surgery.

Postoperative nausea and vomiting (PONV) is a common and challenging complication[1] that has been widely researched. According to the literature, the main risk factors for PONV are female sex, perioperative administration of opioids, type of surgery, use of volatile anesthetics, a history of PONV or motion sickness, nonsmoking status, duration of anesthesia, and younger age.[2,3] The more risk factors a patient has, the higher their risk for PONV.[3] Propofol-based total intravenous anesthesia (TIVA), which does not include volatile (inhalational) anesthetics, has been shown to reduce the risk of PONV among high-risk patients undergoing general anesthesia.

It has been reported that the effect of inhalational anesthesia (IA) on PONV is particularly prominent within the first 2 hours following surgery.[4,5] On the other hand, patients receiving TIVA have been shown to have a higher risk of late PONV, defined as PONV starting 2 to 6 hours after surgery.[5] These considerations have led us to propose the following general hypothesis for minor oral surgery patients undergoing general anesthesia: 1) early PONV will occur more frequently with IA than with TIVA, and 2) late PONV will occur more frequently with TIVA than with IA.

Even though PONV is typically defined as having an onset within the first 24 hours after surgery, the aim of this study was to determine whether PONV risk factors change depending on the time elapsed from surgery. Therefore, our primary objective was to determine the incidence of overall (onset within 0–24 h), early (onset within 0–2 h), and late (onset within 2–24 h) PONV and identify any significant independent variables for PONV including anesthesia type (IA vs TIVA) and known risk factors[3] identified in the reported literature. Secondary objectives were as follows: 1) to compare PONV data based on anesthesia type to identify risk factor differences assuming that anesthesia type was identified as an independent factor for PONV; 2) to calculate odds ratios (OR) for independent variables adjusting for confounding factors for overall, early, and late PONV; 3) to analyze any differences in PONV onset (early vs late); and

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4) to compare the need for rescue antiemetics for the overall, early, and late periods.

METHODS

This retrospective cohort study was approved by the Institutional Review Board (approval number 2023-010) of Saitama Medical University Hospital and adhered to the guidelines of the Declaration of Helsinki. All methods were performed in accordance with relevant guidelines and regulations, and informed consent was obtained from all subjects.

The clinical data of patients who received general anesthesia for minor oral surgery from January 5, 2021, to July 31, 2022, were examined. The inclusion criteria consisted of patients who were between 16 and 85 years of age and underwent intubated general anesthesia with either IA or TIVA. The exclusion criteria consisted of antiemetic treatment within 24 hours prior to the operation and any neurological or psychological disorders.

The protocol for inducing general anesthesia was not fixed and was determined by each anesthesiologist arbitrarily. Analgesics and antiemetics were administered intraoperatively and postoperatively based on patient need as determined by the anesthesiologists or the ward dentists. Immediately prior to all surgeries, infiltration anesthesia was administered using several milliliters of 1% lidocaine with 1:100,000 epinephrine in the surgical field, and the amount of blood loss was noted in the anesthesia record. The same observer interviewed all patients at 2, 6, and 24 hours postoperatively and recorded PONV data along with the use of postoperative analgesics and antiemetics on the postoperative checklists as a daily clinical practice.

The primary outcomes of this study were PONV overall, early, and late. For this study, PONV was defined as an episode of nausea and/or vomiting experienced by a patient during the first 24 hours after surgery. Per Apfel et al,[4] any PONV that occurred across 2 periods was categorized in each period.

Potential risk factors for PONV as identified in the reported literature[2,3] as independent variables were recorded. Data were collected from the postoperative checklists, anesthesia records, nursing charts, and the operation theater notes and were divided into 3 sections: 1) patient-, 2) anesthesia-, and 3) surgery-related factors.

The following patient-related demographic factors were examined for comparison between the PONV and non-PONV groups: age, body mass index (BMI), sex, Apfel score, American Society of Anesthesiologists Physical Status (ASA-PS), smoking status, and history of PONV or motion sickness. For comparison between anesthesia type (IA or TIVA) and for univariate analysis, age (<50 y), BMI (<25 kg/m^2), female sex, Apfel score, ASA-PS, smoking status, and history of PONV or motion sickness were examined as patient-related factors. Apfel scores were calculated based on sex (female), nonsmoking status, history of PONV or motion sickness, and postoperative opioid use and were categorized as low (0–1), mild (2), and high (3–4).[3]

The following anesthesia-related factors were examined for comparison between the PONV and non-PONV groups: use of intraoperative antiemetics, duration of anesthesia, intraoperative fentanyl use and dose, and anesthesia type. For comparison between anesthesia type and for univariate analysis, use of intraoperative antiemetics, duration of anesthesia (>2 hours), intraoperative fentanyl use, and use of IA were examined as anesthesia-related factors.

The surgery-related factors were surgery type and consisted of either tooth extraction or others.

Statistical Analysis

The Mann–Whitney *U* test was used for comparison of continuous variables for the occurrence of PONV, and Fisher exact test was used for categorical variables. The Kruskal-Wallis test was used for comparison of categorical variables in 3 groups, such as the 3 rating scores used in the Apfel score, for the incidence of PONV. If there were statistically significant differences among the 3 groups used in the Kruskal-Wallis test, the Bonferroni post hoc test was performed to analyze whether there were statistically significant differences between each group, such as Apfel scores 1 and 2.

Univariate logistic regression analysis and multivariate logistic regression analysis were performed to assess the independent correlations between the incidence of PONV and several collected patient characteristics. We used a multivariate logistic regression analysis adjusted for age (<50 years), female sex, use of intraoperative antiemetics, intraoperative fentanyl use, and use of IA as independent variables as described in previous literature[3] to assess the probability of PONV occurrence by calculating the OR.

For statistical analysis, continuous variables are presented as the means ± SDs. The normality of our data was assessed using the Shapiro–Wilk test. A $P < .05$ was considered statistically significant. All statistical analyses were performed using EZR software (ver. 1.61) for Windows,[6] which is available for free on the website (http://www.jichi.ac.jp/saitama-sct/SaitamaHP.files/statmed.html).

RESULTS

There were 250 cases who met the inclusion criteria; however, 62 cases had some missing data and were excluded. No cases were excluded based on the exclusion criteria. Therefore, data from a total of 188 patients were included in the analysis. Patient characteristics are shown in Table 1. All patients in this study underwent minor oral surgery under intubated general anesthesia with remifentanil, and all were fully awake and oriented (Ramsay scale 2), had stable vital signs, and minimal

Table 1. Risk Factors and Overall PONV

	Total (N = 188)	*PONV (n = 41)*	*No PONV (n = 147)*	*P value*
Patient-related factors				
Age, mean (SD), y	46.5 (20.2)	42.8 (21.6)	47.5 (19.8)	.277
BMI, mean (SD), kg/m^2	22.8 (3.4)	22.5 (3.4)	22.9 (3.4)	.278
Sex, female/male, No.	100/88	31/10	69/78	.001*
Apfel score, 0–1 (low risk)/2 (mild risk)/3 (high risk), No.[a]	96/74/18	12/21/8	84/53/10	.006*
ASA-PS, 1/2/3, No.	83/94/11	19/18/4	64/76/7	.774
Smoking status, y/n, No.	53/135	10/31	43/104	.535
History of PONV or motion sickness, y/n, No.	33/155	11/30	22/125	.132
Anesthesia-related factors				
Use of intraoperative antiemetics, 0/1/2+, No.	44/134/10	8/29/4	36/105/6	.474
Duration of anesthesia, mean (SD), min	108.8 (41.8)	115.2 (45.1)	107 (40.9)	.364
Intraoperative fentanyl dose, mean (SD), μg	104.4 (124.0)	104.3 (172.5)	104.4 (125.4)	.918
Anesthesia type, IA/TIVA, No.	98/90	29/12	69/78	.008*
Surgery-related factors				
Surgery type, tooth extraction/others, No.	94/94	19/22	75/72	1.0

* Indicates $P < .05$.

[a] Statistically significant difference among low-, mild-, and high-risk groups between those with and without PONV. $P = .006$ for low-risk group vs high- and mild-risk groups in overall period.

Abbreviations: PONV, postoperative nausea and vomiting; BMI, body mass index; ASA-PS, American Society of Anesthesiologists Physical Status; IA, inhalational anesthesia; TIVA, total intravenous anesthesia; Overall, 0–24 h.

pain when leaving the operating room. No opioids were used for postoperative analgesia; however, flurbiprofen or acetaminophen were used. The amount of bleeding was less than 50 mL in all cases.

PONV Rates and Risk Factors

A total of 41 patients (21.8%) developed overall PONV, 35 patients (18.6%) had early PONV, and 14 patients (7.4%) had late PONV (Tables 1 and 2).

Regarding patient-, anesthesia-, and surgery-related factors, only sex, Apfel score, and anesthesia type were identified as significant factors for overall and early PONV, while only sex and Apfel score were associated with significantly higher late PONV. More females than males had PONV overall (31.0% vs 11.4%, respectively; $P = .001$; Table 1), early (26.0% vs 10.2%, respectively; $P = .023$; Table 2), and late (12.0% vs 2.3%, respectively; $P = .037$; Table 2). Increased Apfel scores significantly correlated with higher rates of PONV overall (low vs mild vs high risk; 12.5% vs 28.4% vs 44.4%,

Table 2. Risk Factors for Early and Late PONV

	Early (N = 188)			*Late (N = 188)*		
	PONV (n = 35)	*No PONV (n = 153)*	*P value*	*PONV (n = 14)*	*No PONV (n = 174)*	*P value*
Patient-related factors						
Age, mean (SD), y	42.1 (21.7)	47.5 (19.9)	.172	44.0 (28.2)	46.6 (19.7)	.447
BMI, mean (SD), kg/m^2	22.7 (3.4)	22.9 (3.5)	.435	23.2 (7.1)	22.7 (16.1)	.364
Sex, female/male, No.	26/9	74/79	.023*	12/2	88/86	.037*
Apfel score, 0–1 (low risk)/2 (mild risk)/3 (high risk), No.[a]	11/18/6	85/56/12	.001*	4/6/4	92/68/14	.030*
ASA-PS, 1/2/3, No.	18/14/3	65/80/8	.976	5/7/2	78/87/9	.355
Smoking status, y/n, No.	8/27	45/108	.438	2/12	51/123	.356
History of PONV or motion sickness, y/n, No.	9/26	24/129	.322	4/10	29/145	.275
Anesthesia-related factors						
Use of intraoperative antiemetics, 0/1/2+, No.	7/24/4	37/110/6	.352	2/12/0	42/122/10	.461
Duration of anesthesia, mean (SD), min	114.0 (43.3)	107.5 (41.6)	.423	99.7 (48.1)	107.9 (41.4)	.585
Intraoperative fentanyl dose, mean (SD), μg	90.7 (111.8)	107.5 (126.7)	.572	162.5 (146.6)	100.3 (121.7)	.086
Anesthesia type, IA/TIVA, No.	25/10	73/80	.034*	8/6	90/84	.785
Surgery-related factors						
Surgery type, tooth extraction/others, No.	17/18	77/76	1.00	9/5	86/88	.406

* Indicates $P < .05$.

[a] Statistically significant difference among low-, mild-, and high-risk group between those with and without PONV. $P = .001$ for low-risk group vs high- and mild-risk group in early period. $P = .030$ for low-risk group vs high-risk group in late period.

Abbreviations: PONV, postoperative nausea and vomiting; BMI, body mass index; ASA-PS, American Society of Anesthesiologists Physical Status; IA, inhalational anesthesia; TIVA, total intravenous anesthesia; Early, 0–2 h; Late, 2–24 h.

Table 3. Comparing Overall PONV for IA vs TIVA

	IA (n = 98)	*TIVA (n = 90)*	*P value*
Incidence of PONV, No. (%)	29 (29.6)	12 (13.3)	.008*
PONV, y/n, No.	29/69	12/78	.017*
Patient-related factors			
Age, <50/≥50 y, No.	45/53	52/38	.104
BMI, <25/≥25 kg/m^2, No.	26/72	20/70	.432
Sex, female/male, No.	46/52	54/36	.970
Apfel score, 0–1 (low risk)/2 (mild risk)/3 (high risk), No.	50/41/7	46/33/11	.782
ASA-PS, 1/2/3, No.	37/52/9	36/42/2	.052
Smoking status, y/n, No.	32/66	21/69	.156
History of PONV or motion sickness, y/n, No.	18/80	15/75	.759
Anesthesia-related factors			
Use of intraoperative antiemetics, 0/1/2+, No.	27/67/4	17/67/6	.228
Duration of anesthesia >2 h, y/n, No.	29/69	28/62	.821
Intraoperative fentanyl use, y/n, No.	49/49	42/48	.648
Surgery-related factors			
Surgery type, tooth extraction/others, No.	50/48	44/46	.770

* Indicates $P < .05$.

Abbreviations: PONV, postoperative nausea and vomiting; IA, inhalational anesthesia; TIVA, total intravenous anesthesia; BMI, body mass index; ASA-PS, American Society of Anesthesiologists Physical Status; Overall, 0–24 h.

respectively; $P = .006$; Table 1), early (11.5% vs 24.3% vs 33.3%, respectively; $P = .001$; Table 2), and late (4.2% vs 8.1% vs 22.2%, respectively; $P = .030$; Table 2). IA had a significantly higher incidence compared with TIVA for PONV overall (29.6% vs 13.3%, respectively; $P = .008$; Table 1) and early (25.5% vs 11.1%, respectively; $P = .034$; Table 2). All other analyzed variables were found to be insignificant.

No significant differences were found when comparing overall PONV data with respect to anesthesia type (Table 3).

Calculated Odds Ratios

Using univariate and multivariate analyses, calculated OR revealed the probability of developing PONV overall, early, and late was 2.5 to 6 times higher for females compared with males ($P < .05$; Tables 4 and 5). Increasing Apfel scores also had roughly 2.5 times higher rates of overall, early, and late PONV ($P < .05$; Table 4). Moreover, the probability of developing overall and early PONV was approximate 3 times higher for IA compared with TIVA, but not late PONV ($P \leq .05$; Tables 4 and 5).

Table 4. Univariate Analysis of Patient-, Anesthesia-, and Surgery-Related Risk Factors for Overall, Early, and Late PONV

	Overall (N = 188)		*Early (N = 188)*		*Late (N = 188)*	
	OR (95% CI)	*P value*	*OR (95% CI)*	*P value*	*OR (95% CI)*	*P value*
Patient-related factors						
Age, <50 y vs ≥50	1.39 (0.69–2.81)	.354	1.28 (0.61–2.69)	.511	1.74 (0.56–5.40)	.339
BMI >25 vs ≤ 25 kg/m^2	0.7 (0.30–1.66)	.423	0.75 (0.30–1.85)	.524	0.81 (0.22–3.05)	.763
Sex, female vs male	2.46 (1.13–5.33)	.022*	2.33 (1.04–5.22)	.040*	5.86 (1.27–27.0)	.048*
Apfel score, 0–1 (low risk)/2 (mild risk)/3 (high risk), No.	2.45 (1.45–4.14)	.001*	2.23 (1.30–3.85)	.004*	2.54 (1.17–5.51)	.030*
ASA-PS (1/2/3)	1.06 (0.60–1.90)	.835	0.85 (0.46–1.59)	.615	1.65 (0.68–4.02)	.273
Smoking status, y vs n	0.94 (0.44–2.013)	.561	1.41 (0.60–3.33)	.438	2.49 (0.54–11.5)	.244
History of PONV or motion sickness, y vs n	2.08 (0.91–4.76)	.817	1.86 (0.78–4.46)	.164	2.00 (0.59–6.82)	.268
Anesthesia-related factors						
Use of intraoperative antiemetics, y vs n	1.46 (0.71–3.03)	.306	1.51 (0.69–3.27)	.303	1.25 (0.40–3.88)	.699
Duration of anesthesia, >2 h vs ≤2 h	1.44 (0.70–2.99)	.325	1.46 (0.68–3.16)	.332	1.30 (0.42–4.08)	.649
Intraoperative fentanyl, y vs n	1.16 (0.58–2.31)	.683	1.16 (0.58–2.31)	.683	2.02 (0.65–6.27)	.224
Anesthesia type, IA vs TIVA	2.73 (1.29–5.76)	.008*	2.74 (1.2–6.09)	.013*	1.24 (0.41–3.74)	.697
Surgery-related factors						
Surgery type, tooth extraction vs others	1.37 (0.68–2.74)	.378	1.24 (0.59–2.58)	.574	1.43 (0.44–4.68)	.552

* Indicates $P < .05$.

Abbreviations: PONV, postoperative nausea and vomiting; OR, odds ratio; CI, confidence interval; BMI, body mass index; ASA-PS, American Society of Anesthesiologists Physical Status; IA, inhalational anesthesia; TIVA, total intravenous anesthesia; Overall, 0–24 h; Early, 0–2 h; Late, 2–24 h.

Table 5. Multivariate Analysis of Related Factors for Overall, Early, and Late PONV

	Overall (N = 188)		*Early (N = 188)*		*Late (N = 188)*	
	OR (95% CI)	*P value*	*OR (95% CI)*	*P value*	*OR (95% CI)*	*P value*
Age, <50 y vs ≥50	1.24 (0.56–2.75)	.598	1.16 (0.50–2.67)	.733	1.36 (0.40– 4.64)	.626
Sex, female vs male	3.01 (1.36–6.65)	.006*	2.57 (1.12–5.88)	.025*	6.20 (1.30–29.5)	.041*
Use of intraoperative antiemetics, y vs n	1.15 (0.47–2.81)	.765	1.21 (0.47–3.12)	.688	0.79 (0.22– 2.87)	.722
Intraoperative fentanyl, y vs n	1.13 (0.54–2.38)	.738	0.97 (0.45–2.11)	.942	2.21 (0.67–7.31)	.196
Anesthesia type, IA vs TIVA	2.97 (1.37–6.45)	.006*	2.94 (1.29–6.70)	.010*	1.24 (0.40–3.87)	.708

* Indicates $P < .05$.

Abbreviations: PONV, postoperative nausea and vomiting; OR, odds ratio; CI, confidence interval; IA, inhalational anesthesia; TIVA, total intravenous anesthesia; Overall, 0–24 h; Early, 0–2 h; Late, 2–24 h.

PONV Onset

Looking at the onset of PONV, approximately 85% (35/41 patients) had early PONV while only 14.6% (6/41 patients) had late PONV ($P < .001$; Table 6). Within group differences for early and late PONV were statistically significant for both the IA ($P = .002$; Table 6) and TIVA ($P = .032$; Table 6) groups; however, differences for early and late PONV between the IA and TIVA groups were not statistically significant ($P > .05$). Similar results were shown for sex (Table 6).

Antiemetics

An increased number of intraoperative antiemetics had no correlation with the incidence of PONV in the present study (Tables 1, 2, 4, and 5). Although not included in detail in this study, the rates of prophylactic antiemetic use are shown in Table 7, and dexamethasone alone was the most common strategy, given in approximately 70% of the total cases (132/188).

No statistically significant differences were demonstrated between IA and TIVA groups or based on sex for rescue antiemetic (metoclopramide) use in either the overall, early, or late periods (Table 8).

DISCUSSION

A primary objective of this study was to determine the incidence of overall, early, and late PONV in patients undergoing minor oral surgery. It is well known that the incidence of PONV is higher in patients who undergo major oral surgery, such as orthognathic surgery, than in those who undergo minor oral surgery.[7–11] The incidence of overall PONV was 21.8% in the present study which was consistent with previous reports for minor oral surgery.[8,10,11] However, although dental surgery is not included among the surgery-related risk factors for PONV, the incidence and course of PONV vary depending on the surgical technique.[7,9,10] Since some surgical procedures are reported to be high-risk for PONV,[7,9] it will be necessary to establish a consensus on high-risk surgical procedures.

From statistical analyses used in our study, female sex and use of IA were identified as significant risk factors for PONV. Moreover, females had a significantly higher incidence of overall, early, and late PONV than males. Use of IA had a significantly higher incidence of overall and early PONV only, although neither anesthesia type had a strong correlation with late PONV. Interestingly, fentanyl use had no significant correlation with PONV and anesthesia type despite nearly 50% in each group not receiving intraoperative fentanyl. These results suggested that PONV risk factors, particularly anesthesia type, might vary depending on the time elapsed following minor oral surgery.

There have been several reports that the Apfel score is useful for predicting PONV after oral surgery,[3,7,8,12,13] while other studies have found differing results.[9,10,14] This could be due to differences in patient factors, such as younger age, and special conditions, such as postoperative restrictions. Our present study demonstrated that increased Apfel scores were correlated with an increased incidence of overall, early, and late

Table 6. Comparing Early and Late Onset of PONV

	Overall PONV (n = 41)	*Early PONV (n = 35)*	*Late PONV (n = 6)*	*P value*
PONV onset, No. (%)	41 (100)	35 (85.4)	6 (14.6)	<.001
PONV onset vs anesthesia type				
PONV onset for IA, No. (%)	29 (100)	25 (86.2)	4 (13.8)	.002
PONV onset for TIVA, No. (%)	12 (100)	10 (83.3)	2 (16.7)	.032
PONV onset vs sex				
PONV onset for female, No. (%)	31 (100)	26 (83.9)	5 (16.1)	.002
PONV onset for male, No. (%)	10 (100)	9 (90.0)	1 (10.0)	.018

P value demonstrates comparison of early vs late PONV. PONV onset reflects the first occurrence of PONV. Abbreviations: PONV, postoperative nausea and vomiting; IA, inhalational anesthesia; TIVA, total intravenous anesthesia; Overall, 0–24 h; Early, 0–2 h; Late, 2–24 h.

Table 7. Accounting of Prophylactic Antiemetics

Antiemetic agent(s)	*Total cases (N = 188)*
Dexamethasone alone	132
Droperidol alone	1
Metoclopramide alone	1
Dexamethasone plus droperidol	4
Metoclopramide plus dexamethasone	6

As prophylactic antiemetics, dexamethasone and droperidol were administered before surgery started, while metoclopramide was given near the end of surgery.

PONV. The results were found to be useful in predicting PONV, perhaps because the subjects in the present study did not have any postoperative restrictions or receive nasogastric evacuation.

Our results reconfirmed that general anesthesia with IA is also a risk factor for overall PONV and that propofol may be useful in reducing the incidence of PONV in minor oral surgery patients. However, some studies have prompted a reconsideration of propofol's usefulness for PONV. Hasegawa et al[10] reported that the OR of PONV was 13 times higher with IA than with TIVA used in patients undergoing extraction of their wisdom teeth. In contrast, it has been reported that there is no difference in the incidence of PONV between IA and TIVA for the same surgery.[15] Moreover, although orthognathic surgery was performed, a significantly higher rate of PONV was observed in patients with TIVA than in patients with sevoflurane anesthesia.[8] In addition, Pourtaheri et al[13] showed no significant correlations between PONV and the use of a propofol drip. Therefore, as there might be no consensus, future studies on anesthesia for oral surgery are expected.

There are few reports comparing IA and TIVA in terms of early and late PONV in oral surgery patients. It has been reported that the frequency of PONV was higher in patients with IA than in patients with TIVA within 60 minutes after surgery.[11] Furthermore, in a study that divided the postoperative period into early (0–6 h) and late periods (6–24 h), IA significantly increased the frequency of PONV in the early period when compared to TIVA, while there was no difference in the frequency of PONV between patients with IA and those with TIVA in the late period.[12] Our study is consistent with these reports.

These results supported our hypothesis, in part, because IA demonstrated a significantly higher incidence of PONV than TIVA in the early period. However, we also found that TIVA did not significantly increase the incidence of late PONV compared with IA (Table 2). Possible reasons why our study showed results different from our hypothesis are as follows: 1) Based on our hypothesis, it is possible that the effect of propofol, which generally has antiemetic properties,[16] masked PONV symptoms likely caused by patient-, anesthesia-, and surgery-related factors in the early period, while in the late period, the effect of propofol had disappeared,[16] and each related risk factor was no longer masked. 2) In the present study, only sex (female) and increasing Apfel score were found to be associated with increased late PONV, suggesting that the risk for late PONV did not increase with TIVA even after the effect of propofol disappeared. As a result, it is possible that the emetogenic effect of IA also disappeared later,[4] which may explain why the frequency of late PONV was equivalent for both IA and TIVA. However, further studies are needed regarding our present hypothesis because the detailed mechanisms of propofol's antiemetic actions and IA's emetogenic actions are still unclear.[4,16]

PONV Onset

Regarding the timing of initial PONV episodes, we found that PONV primarily occurred early (~85%; 35/41) as opposed to late (~15%; 6/41), a consistent trend regardless of anesthesia type or sex (Table 6). Although PONV is defined as nausea and vomiting occurring within 24 hours after surgery, we found that PONV initially occurs more frequently within 2 hours after minor oral surgery regardless of whether IA or TIVA was used. Studies of PONV risk factors have examined the 24- to 48-hour postoperative period, but very few have subdivided the 24-hour period.

There have been few reports on PONV after oral surgery, especially regarding the timing of initial PONV episodes and associated risk factors. Silva et al[7] examined the frequency

Table 8. Rescue Antiemetics for Early and Late PONV

	Overall	*P value*	*Early*	*P value*	*Late*	*P value*
Rescue antiemetics vs anesthesia type						
IA, No. (%)	12/29 (41.4)	.371	7/25 (28.0)	.328	5/8 (62.5)	.443
TIVA, No. (%)	3/12 (25.0)		1/10 (10.0)		2/6 (33.3)	
Rescue antiemetics vs sex						
Female, No. (%)	13/31 (41.9)	.310	7/26 (26.9)	.390	6/12 (50.0)	.753
Male, No. (%)	2/10 (20.0)		1/9 (11.1)		1/2 (50.0)	

P value demonstrates comparison between groups for antiemetic (metoclopramide) rescue. Numerator is antiemetic use, and denominator is total patients who complained of PONV. No patient received rescue antiemetic more than twice. Abbreviations: IA, inhalational anesthesia; TIVA, total intravenous anesthesia; Overall, 0–24 h; Early, 0–2 h; Late, 2–24 h.

of PONV after general anesthesia with IA and found that the incidence of PONV at 2 hours was 75% and 1.3% after 5 hours. Şimşek et al[11] examined the occurrence of PONV within 60 minutes and found that PONV was approximately 2.5 times more frequent following recovery from sevoflurane-based IA than following recovery from TIVA. Albuquerque et al[17] found that 60% of all cases of PONV occurred within 2 hours after general anesthesia with mainly IA. Gecaj-Gashi et al[12] reported that more than half of PONV patients developed PONV within 6 hours under general anesthesia with either IA or TIVA. Ishikawa et al[18] found that the incidence of PONV in patients who received TIVA with propofol was 2.7 times higher at 2 to 24 hours than that at 0 to 2 hours. Therefore, reports of PONV occurring in the early period are consistent with our results especially with IA,[7,11,12,17] but there are reports of increased late PONV after TIVA which contradict our results.[18] The findings in the study by Ishikawa et al[18] may differ from ours because their study included a major oral surgery and younger patients. Regarding the incidence of late PONV with TIVA, although our present study which included relatively older subjects undergoing minor oral surgery did not support our hypothesis in full, the study by Ishikawa et al[18] suggests our hypothesis may be correct.

Antiemetics

It is well known that intraoperative and postoperative antiemetics reduce the incidence of PONV.[2,13,18] However, the results of the current study suggested that neither intraoperatively nor postoperatively administered antiemetics had any statistically significant correlation with PONV incidence (Tables 1, 2, 4, 5, and 8). The antiemetic agents that are used in our institution are metoclopramide, droperidol, and dexamethasone (Table 7). Ondansetron began being covered by insurance in Japan on February 25, 2022, but it had not yet been used at our institution in July 2022.

In general, it is known that the antiemetic effect of 10 mg of metoclopramide is uncertain and that droperidol (0.625–1.25 mg) is effective for preventing PONV (Evidence A1).[20] Furthermore, perioperative dexamethasone has long been used to reduce the incidence of PONV.[20] Weibel et al[19] stated that dexamethasone has a high strength of evidence for the prevention of postoperative emesis and that droperidol has a moderately high strength of evidence. Although the types of antiemetics were the same as those used in the study by Ishikawa et al,[18] more patients received 1 antiemetic (dexamethasone), and fewer patients received multiple antiemetics compared with their study (Table 7). According to the literature,[7,20] prophylaxis with a single antiemetic is less effective in high-risk PONV patients, and thus, a combination of multiple antiemetics is recommended. Therefore, although there were no cases of difficult PONV management and the optimal number of combined antiemetics remains unclear,[21] the potential for undertreating PONV should be recognized. Although inconsistent with our present results and a previous study in which the administration of antiemetics did not correlate with PONV,[4] it is possible that the incidence of PONV in this study could have been reduced if more combined antiemetics, such as droperidol, dexamethasone, and ondansetron, were administered.

Limitations and Strength

This study has several limitations. First, it was a retrospective cohort study, and analgesics and antiemetics were administered postoperatively whenever PONV became intolerable rather than just for PONV prophylaxis which could have led to bias. Larger controlled studies are needed to further evaluate the incidence of PONV and its effects on the clinical outcomes of patients undergoing surgery. Second, this was a single-center study, and the results might not be generalizable. Third, it is well understood that multivariate analysis with a small number of cases will reduce statistical power, so it is possible that our calculated sample size (N = 188) was insufficient to support that type of statistical analysis. Given that we found no difference in late PONV for anesthesia type, this finding may reflect an underpowered study. This may require further study with a larger sample of patients undergoing minor oral surgery.

However, there are strengths in our present study. In retrospective cohort studies, it is often easy to miss PONV because data are often taken from medical records. In the current study, patients were interviewed about PONV at 2, 6, and 24 hours. Therefore, compared with other retrospective studies, this is likely a more accurate reflection of PONV.

CONCLUSION

Our study found that IA was significantly associated with increased overall and early PONV, but not late PONV, as compared with TIVA which partially supports our hypothesis. The only other significant PONV risk factors were female sex and increased Apfel scores which correlated with overall, early, and late PONV. There were no differences in identified PONV risk factors based on anesthesia type, and most patients with PONV experienced early PONV as opposed to late PONV. This study's results suggested that anesthesia type being a PONV risk factor may change depending on the postoperative period being assessed.

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