Retrospective Study on the Incidence of Postoperative Nausea and Vomiting and Hypotension During Orthognathic Surgery Using Propofol or Remimazolam

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Objective: This study aimed to evaluate the incidence of early (up to 2 h) and late (2–24 h) postoperative nausea and vomiting (PONV) and hypotension in patients who underwent general anesthesia for orthognathic surgery using propofol or remimazolam along with remifentanil.

Methods: This retrospective chart review included healthy adult patients under the age of 60 who underwent orthognathic surgery using propofol (P group) or remimazolam (R group) from January 2021 to March 2022. Records were reviewed to gather PONV and intraoperative hypotension data as well as patient characteristics and other variables.

Results: Early PONV was significantly lower in the P group vs the R group (9.5% vs 34.1%, respectively; $P = .002$), although the difference in late PONV was insignificant (36.9% vs 51.2%, respectively; $P = .13$). A higher incidence of intraoperative hypotension was noted in the P group (22.6%) vs the R group (2.4%; $P = .004$); however, there were no differences in average intraoperative systolic blood pressure or vasopressor administration.

Conclusion: These results suggest that propofol is associated with a lower incidence of early PONV as compared to remimazolam; however, antiemetics are still recommended given the frequency of late PONV in both groups. Propofol also caused more episodes of intraoperative hypotension vs remimazolam, but the increase in transient hypotension is likely to be irrelevant during orthognathic surgery in healthy adults under the age of 60.

Key Words: Remimazolam; Propofol; Postoperative nausea and vomiting (PONV); Intraoperative blood pressure; Orthognathic surgery.

Postoperative nausea and vomiting (PONV) after general anesthesia is a distressing and unpleasant postoperative complication for patients. The incidence of PONV is reported to approximate 36% (18%–45%).[1] However, the actual incidence of PONV following orthognathic surgery is estimated to be even higher (40%–67%) due to the large number of young female orthognathic patients and the bleeding that can occur during and after surgery.[2–4] In addition, because orthognathic surgery often necessitates postoperative limitations on mouth opening including intermaxillary fixation, vomiting may cause serious complications such as airway obstruction and pulmonary aspiration. To reduce these risks, general anesthesia for orthognathic surgery at our institution is often maintained with a combination of propofol and remifentanil.

Propofol has antiemetic effects,[5] and remifentanil can reduce intraoperative bleeding by reducing oral tissue blood flow due to potent hypotensive effects and less peripheral vasodilation.[6–10] Propofol reduces the incidence of PONV compared with inhaled anesthetics.[11,12] However, it has been reported that intraoperative hypotension is likely to occur due to sympathetic inhibitory effects and impairment of baroreflex regulatory mechanisms.[13] Conversely, remimazolam, a new ultrashort-acting intravenous (IV) benzodiazepine, provides improved hemodynamic stability and is less likely to lower blood pressure compared to propofol.[14]

Although known PONV risk factors include females, nonsmokers, history of PONV/motion sickness, and postoperative

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opioid use, intraoperative hypotension may be another risk factor.[15] It is not clear whether remimazolam and propofol have different effects on PONV following orthognathic surgery.

We previously investigated the incidence of PONV and intraoperative blood pressure in patients who underwent orthognathic surgery under total intravenous anesthesia (TIVA) with a combination of propofol or remimazolam and remifentanil. The average intraoperative systolic blood pressure was 102.1 ± 8.2 mm Hg in the propofol group and 107.9 ± 8.2 mm Hg in the remimazolam group, a statistically significant difference that likely lacked clinical relevance.[16] We also investigated the incidence of PONV up to 30 minutes (early postoperative period) and 12 hours (late postoperative period) after surgery. We reported a significantly lower incidence of early PONV in the propofol group.[16] However, many studies defined early postoperative period as up to 2 hours postoperatively and observed patients for PONV up to 24 hours postoperatively.[12,17,18] Hence, it is possible that our previous study failed to accurately reflect the incidence of PONV due to the short time periods covered.

Therefore, in this study we increased the number of cases and changed the target periods for the early (up to 2 h) and late (2–24 h) postoperative periods for participants who underwent orthognathic surgery under TIVA using propofol or remimazolam along with remifentanil. Our primary objectives were to retrospectively compare the incidence of early and late PONV and assess any episodes of hypotension between the 2 anesthetics.

METHODS

This retrospective chart review was approved by the Ethics Committee of Tokyo Dental College (approval number: 1065). Patients who underwent 1-jaw surgery (bilateral sagittal split ramus osteotomy) or 2-jaw surgery (LeFort I osteotomy and bilateral sagittal split ramus osteotomy) under TIVA with propofol (P group) or remimazolam (R group) as well as remifentanil at our institution during the 15-month period from January 2021 to March 2022 were included. Patients with hypertension, bleeding disorders, on antithrombotic drugs, aged 60 years or older, and with an American Society of Anesthesiologists physical status (ASA-PS) of 3 or higher were excluded. In addition, none of the patients received elective hypotensive anesthesia during surgery.

Medical and anesthesia records were reviewed retrospectively. The surveyed items were as follows: age, sex, weight, body mass index, ASA-PS, smoking history, history of PONV/motion sickness, resting systolic blood pressure on the day before surgery, surgical procedure, operation time, anesthesia time, total local anesthetic dose, total intraoperative remifentanil dose, total intraoperative fentanyl dose, use and total dose of postoperative opioids, average intraoperative systolic blood pressure, intraoperative hypotension (defined as systolic blood pressure <80 mm Hg), intraoperative vasopressor use, intraoperative bleeding, early and late PONV (up to 2 h after surgery and 2–24 h after surgery, respectively), antiemetic use, and flumazenil use in the R group. An Apfel score was calculated for each patient based on risk factors (females, nonsmokers, history of PONV/motion sickness, and postoperative opioid use) to determine their degree of PONV risk.

The average intraoperative systolic blood pressure was calculated using the noninvasively measured systolic blood pressure values obtained at 5-minute intervals from the start of the operation until the end. The blood pressure coefficient of variation (CV) was calculated by dividing the standard deviation by the average value of systolic blood pressure at 5-minute intervals. PONV was determined based on nursing records and was divided into early and late periods. Patients who complained of nausea or vomiting were considered to have PONV.

Statistical Analysis

Statistical analyses were performed using the χ^2 test and the Mann–Whitney U test. A P value of less than .05 was considered significant. Data were expressed as mean ± standard deviation. SPSS software (version 28, IBM) was used for statistical analyses.

A post-hoc power analysis was performed to calculate the statistical power of the incidence of early and late PONV between the 2 groups with a total sample size of 125 and an α error of .05.

RESULTS

A total of 126 target cases were identified, 1 case was excluded as the patient had hypertension, 84 cases were included in P group, and 41 cases were in R group. There were no significant differences between the 2 groups in terms of patient characteristics (Table 1).

Looking at the measured variables, there were no significant differences between the 2 groups other than early PONV and intraoperative hypotension (Table 2). The incidence of early PONV was significantly lower in the P group (9.5%) than in the R group (34.1%; $P = .002$; statistical power of 86%). Although late PONV was lower in the P group (36.9%) than in the R group (51.2%), this difference lacked statistical significance ($P = .13$; statistical power of 27%).

The incidence of intraoperative hypotension (systolic blood pressure <80 mm Hg) was significantly lower in the R group than the P group (2.4% vs 22.6%, respectively; $P = .004$).

Table 1. Patient Characteristics

	P group (n = 84)	*R group (n = 41)*	*P value*
Age, mean (SD), y	27 (9)	26 (7)	.71
Sex, male/female, No.	26 / 58	11 / 30	.64
Weight, mean (SD), kg	57 (9)	57 (11)	.77
Body mass index, mean (SD), kg/m^2	21.1 (2.7)	24.5 (7.0)	.54
ASA-PS 1/2, No.	66 / 18	37 / 4	.17
Smoking history, ±, No.	11 / 73	5 / 36	.89
History of PONV/motion sickness, ±, No.	30 / 54	19 / 22	.25
Resting systolic blood pressure, mean (SD), mm Hg	108.3 (11)	106.7 (12)	.72

ASA-PS indicates American Society of Anesthesiologists physical status; PONV, postoperative nausea and vomiting.

However, the average intraoperative systolic blood pressure was 101.2 ± 7.6 mm Hg in the P group and 109.1 ± 7.8 mm Hg in the R group, lacking both clinical and statistical significance ($P = .59$). Ephedrine (3 cases) or phenylephrine (1 case) were used in the P group, and there were no vasopressors used in the R group; however, this difference lacked statistical significance (Table 2).

Regarding the PONV risk factors, there were no significant differences between the 2 groups for any of the identified factors (Table 3).

In the R group, 11 patients received flumazenil reversal after discontinuation of the remimazolam at the end of surgery.

DISCUSSION

We compared the impacts of propofol and remimazolam on the incidence of early and late PONV and on the average intraoperative systolic blood pressure during orthognathic surgery. The results of this study showed that the incidence of early PONV was significantly lower in the P group, although there was no statistically significant difference in the incidence of late PONV between the 2 groups.

Many reports have been published on the impact of anesthetics on the incidence of PONV. TIVA with propofol reduces the incidence of PONV compared with anesthesia achieved with inhaled anesthetics.[10,11,19] In contrast, some studies have reported that the difference in PONV incidence between propofol and inhaled anesthetics was observed only in the early postoperative period and that there was no difference in PONV incidence thereafter.[12] A comparison of the incidence of PONV between remimazolam and desflurane reportedly showed that the remimazolam group had a significantly lower incidence of PONV in the early postoperative period, while there was no difference in late PONV incidence between those 2 groups.[15] These results suggest that the IV anesthetics propofol and remimazolam suppress PONV more than inhalational anesthetics and that the early antiemetic effect of propofol is stronger than that of remimazolam.

Table 2. Results of Measured Variables

	P group (n = 84)	*R group (n = 41)*	*P value*
Surgical procedure (1-jaw (SSRO)/2-jaws (LF I + SSRO), No.	24 / 60	14 / 27	.52
Operation time, mean (SD), min	202 (76)	216 (82)	.75
Anesthesia time, mean (SD), min	256 (79)	277 (101)	.75
Total local anesthetic dose, mean (SD), mL	27 (5)	26 (6)	.81
Total remifentanil dose, mean (SD), mg	2.8 (1.2)	3.6 (2.5)	.78
Total fentanyl dose, mean (SD), μg	251 (77)	283 (110)	.65
Postop opioid use, No. (%)	60 (71.4)	27 (65.9)	.52
Total postop opioid (fentanyl) dose, mean (SD), μg	200 (196)	260 (314)	.46
Blood loss during surgery mean (SD), mL	170 (145)	255 (266)	.73
PONV early (0–2 h), No. (%)	8 (9.5)	14 (34.1)	.002
PONV late (2–24 h), No. (%)	31 (36.9)	21 (51.2)	.13
Administration of antiemetics, No. (%)	27 (32.1)	18 (43.9)	.20
Intraoperative average systolic blood pressure, mean (SD), mm Hg	101.2 (7.6)	109.1 (7.8)	.59
CV of intraoperative average systolic blood pressure, mean (SD), %	10.2 (3.3)	9.1 (2.6)	.81
Intraoperative hypotension, No. (%)	19 (22.6)	1 (2.4)	.004
Administration of vasopressors, No. (%)	4 (4.8)	0 (0)	.38

SSRO indicates sagittal split ramus osteotomy; LF I, LeFort I osteotomy; PONV, postoperative nausea and/or vomiting; CV, coefficient of variation.

Table 3. Number of PONV Risk Factors

No. of risk factors	*P group (n = 84)*[a]	*R group (n = 41)*[a]	*P value*
0	0 (0)	0 (0)	
1	12 (14.3)	5 (12.2)	
2	24 (28.6)	10 (24.4)	.96
3	30 (35.7)	14 (34.1)	
4	18 (21.4)	12 (29.3)	

[a] No. (%).

The incidence of late PONV in our study was 36.9% in the P group and 51.2% in the R group, but that difference was not found to be statistically significant ($P = .13$). In addition, antiemetic use was 32.1% in the P group and 43.9% in the R group, which also lacked statistical significance. Opioids, a known PONV risk factor, were used postoperatively for many patients (71.4% in the P group and 65.9% in the R group). Pourtaheri et al[3] reported that the incidence of PONV was based on the quantity of postoperative opioids utilized. The quantity of postoperative opioids used in our study were small because we used patient-controlled analgesia with IV fentanyl postoperatively without a continuous infusion setting. In fact, opioid analgesia totals given postoperatively were computed by converting individual doses into IV morphine equivalents (MEQ), and the totals were small (<15.5 MEQ) in both groups. Therefore, it was considered that the incidence of PONV in this study was low relative to the rate of postoperative opioid use. However, approximately 33% of the propofol group and 50% of the remimazolam group still developed late PONV, suggesting that orthognathic surgery carries a high risk for PONV regardless of the type of anesthetic agents utilized.

The average intraoperative systolic blood pressure was 101.2 ± 7.6 mm Hg in the P group and 109.1 ± 7.8 mm Hg in the R group, a difference that lacked both clinical and statistical significance. In addition, there was no difference in CV or intraoperative bleeding. The incidence of intraoperative hypotension was significantly higher in the P group. Intraoperative hypotension has been reported to increase the incidence of PONV.[20,21] However, in the present study, the incidence of early PONV was lower in the P group despite having a significantly higher incidence of hypotension. The reason for this result may be attributable to the lack of a difference in average intraoperative systolic blood pressure and in CV. In other words, transient intraoperative hypotension may not have affected the incidence of early PONV because there were few sustained episodes of hypotension requiring repeated administration of vasopressors.

Doi et al[22] reported that propofol had a significantly higher incidence of intraoperative hypotension than remimazolam: 34.7% in remimazolam group and 60.0% in propofol group. However, the incidence of hypotension in our study was low in both groups: 2.4% in the R group and 22.6% in the P group. In addition, the rate of intraoperative vasopressor use was 4.8% in the P group, illustrating the few cases of sustained hypotension that required vasopressor administration. Kazama et al[23] reported that the decrease in systolic blood pressure due to elevated blood levels of anesthetic agents increases as patient age increases. Since the patients in this study were relatively young, healthy, ASA-PS 1-2 adults below 60 years of age, no difference in average systolic blood pressure between the 2 groups was anticipated for this study.

The results of this study suggest that remimazolam compared to propofol has a lower incidence of intraoperative hypotension but a higher incidence of early PONV. However, approximately one-third to one-half of patients developed late PONV depending on the group. Therefore, in orthognathic surgery, which is considered to have a high risk of PONV, it is necessary to take proactive measures such as the preventive administration of antiemetics regardless of the type of anesthetic agents utilized.

There are several limitations to this retrospective study. First, nausea is a self-reported outcome, and the events were picked up from medical and anesthesia records. Therefore, it is possible that some episodes of nausea were not detected. Second, although the statistical power for the comparison of early PONV incidence between the 2 groups was considerably high, the calculated power for late PONV incidence was quite low. Further studies are needed to evaluate the incidence of late PONV.

CONCLUSION

The results of this retrospective study suggest that the incidence of PONV in the early postoperative period was shown to be lower for TIVA with propofol vs remimazolam. However, given that over 33% of patients still developed late PONV regardless of the anesthetic agent used, it is likely necessary to administer antiemetics prophylactically for orthognathic surgery. On the other hand, there was no significant difference in the average intraoperative systolic blood pressure between TIVA with propofol vs remimazolam during general anesthesia for orthognathic surgery in young, healthy adults.

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