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Nitrous oxide does not aggravate postoperative emesis after orthognathic
surgery in female and non-smoking patients

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Abstract

PURPOSE: The purpose of this study was to evaluate the effect of supplemental nitrous oxide on postoperative nausea and vomiting (PONV) after propofol anesthesia for orthognathic surgery in female and non-smoking patients. **PATIENTS AND METHODS:** We compared PONV in 28 ASA-I female and non-smoking patients undergoing orthognathic surgery. Anesthesia was induced with propofol combined with fentanyl and tracheal intubation was facilitated with vecuronium. Anesthesia was maintained with propofol with or without nitrous oxide. No patient received neostigmine. PONV was assessed as score 0 (no PONV), score 1 (nausea) and score 2 (vomiting) during the 24 hr recovery period. **RESULTS:** There were no differences in patient's characteristics, operation, anesthesia and emergence time, fluid transfusion, blood loss, urine output and total propofol and fentanyl doses between two groups. There was also no difference in PONV score in two groups. Only one patient in each group vomited. **CONCLUSIONS:** It is suggested that supplemental nitrous oxide does not aggravate PONV after propofol anesthesia for orthognathic surgery in female and non-smoking patients.

Key words: postoperative nausea and vomiting, orthognathic surgery, nitrous oxide, propofol

Orthognathic surgery is one of the most common procedures in oral and maxillofacial surgery. Rapid and clear emergence after general anesthesia is important for orthognathic surgery because it is sometimes followed by airway obstruction due to postoperative edema and bleeding. Propofol and sevoflurane are good candidates as an anesthetic because of their rapid emergence profile.¹⁻⁶

Postoperative vomiting is another risk factor for postoperative airway obstruction, especially in patients under intermaxillary fixation. Some anesthetics such as nitrous oxide and volatile anesthetics including sevoflurane, supplemental agents such as opioids, neostigmine, female patient, nonsmoking status and a history of postoperative nausea and vomiting (PONV) are risk factors for PONV.^{7,8} In contrast, since propofol has a strong antiemetic effect after general anesthesia,^{7,8} propofol anesthesia may be a good choice for orthognathic surgery.

Nitrous oxide, despite its emetic effects, produces several advantages such as propofol sparing effects and hemodynamic stability when used with propofol. Nitrous oxide and propofol have an additive interaction in hypnosis⁹ and to suppress pressor responses to stimulations in rabbits.¹⁰

In some studies, it is reported that an addition of nitrous oxide to propofol does not increase the risk of PONV.¹¹⁻¹³ However, there is no report about the effects of supplemental nitrous oxide on PONV after propofol anesthesia for orthognathic surgery, especially in female and non-smoking patients who are at high risk for PONV. In this study, therefore, we investigated PONV after propofol anesthesia with or without nitrous oxide for orthognathic surgery in these patients.

Material and methods

After an institutional approval, 28 female non-smoking patients undergoing Le Fort–1 osteotomy and sagittal splitting mandibular ramus osteotomy participated in the present study. All patients were classified in physical status 1 of the American Society of Anesthesiologists and gave their written informed consent prior to the study. No patient had an experience of general anesthesia before participating this study nor a history of motion sickness. Patients were randomly allocated into one of two groups based on the used anesthetics: propofol group (n=14) and nitrous oxide-propofol group (n=14).

All patients received 0.5 mg atropine sulfate and 2.5–3 mg midazolam as premedication. For induction of anesthesia, patients received 100 mcg fentanyl and 1.5 mg/kg propofol. Nasotracheal intubation was facilitated with 0.1 mg/kg vecuronium bromide. Anesthesia was maintained with 6–10 mg/kg/hr propofol in the propofol group or 60 % nitrous oxide and 6–8 mg/kg/hr propofol in the nitrous oxide-propofol group, respectively, under mechanical ventilation. The standard infusion rate of propofol was 8 mg/kg/hr in the propofol group and 6 mg/kg/hr in the nitrous oxide-propofol group, respectively, during Lefort-1 osteotomy, and 6 mg/kg/hr in both groups during sagittal splitting mandibular ramus osteotomy. However, if increases in indirect blood pressure or heart rate could not be suppressed with supplemental fentanyl as described later, the infusion rate of propofol was increased stepwise by 1 mg/kg/hr. Appropriate doses of 1 % lidocaine solution containing 1:100,000

epinephrine were injected to the surgical field for infiltration anesthesia. All patients received dexamethasone 8 mg to prevent postoperative edema at the start of surgery. Supplemental fentanyl was administered when an increase in indirect blood pressure or heart rate more than 30 % of the control values was observed during surgery. Averages of consecutive two values of blood pressure and heart rate immediately before local anesthetic injection to the surgical field were served as control values. Blood pressure and heart rate were recorded every 2.5 min throughout the anesthesia. Additional vecuronium was used to maintain muscle relaxation until 60 min before the end of surgery. No patient received an agent to reverse the neuromuscular blocking agent at the end of anesthesia. The trachea was extubated after confirming the patient's eye-opening, spontaneous breathing, obeying verbal commands, recovery of protective reflexes, and recovery from muscle relaxation. Acetated Ringer's solution was transfused to keep urine output more than 1 ml/kg/hr throughout the surgery. A 14 Fr. nasogastric drainage tube was inserted to each patient after nasotracheal intubation. The end of the tube was open to the air and removed on the next day of the surgery. After extubation, 3 l/min oxygen was administered via a face mask until 24 hours after extubation. If a patient was suffering from repetitive vomiting after surgery, an administration of droperidol up to 1.25 mg was planned to prevent further vomiting.

Observed variables included operation time, anesthesia time, emergence time (time from the end of surgery to extubation), blood loss during surgery, total fentanyl dose and PONV until 24 hr after surgery. PONV was assessed on the basis of the following scoring criteria. If a patient had no PONV throughout the 24 hr recovery

period, the assessment of the patient was no PONV (score 0). If a patient had nausea at least once but no vomiting during the 24 hr recovery period, the assessment of the patient was nausea (score 1). If a patient had vomiting at least once during the 24 hr recovery period, the assessment of the patient was vomiting (score 2). Assessment was performed by a staff of our department who did not participate in the present study and blinded to the group of the patients. In addition, the number of droperidol administration was recorded during the 24 hr recovery period.

Data are shown as mean \pm standard deviation. Student *t*-test for unpaired samples and Mann-Whitney *u*-test were used for statistical analysis where appropriate. A *p* value less than 5 % was considered as statistically significant.

RESULTS

There were no differences in patient's age, height and body weight between two groups (Table 1). Table 2 shows the data of operation, anesthesia and emergence time, fluid transfusion, blood loss, urine output, total propofol dose and total fentanyl dose in both groups. There were also no differences in operation and anesthesia time, blood loss and hourly urine output between two groups, though data in the propofol group were slightly smaller. Emergence time and hourly fluid transfusion in both groups was quite similar. No differences were observed in total propofol and fentanyl doses, propofol infusion rate and fentanyl dose per body weight between two groups, though data in the nitrous oxide-propofol group were slightly smaller.

PONV scores in both groups are shown in Table 3. Same distribution of

PONV scores was observed in both groups. Only one patient (7.1%) in each group vomited, whereas no patient in both groups received droperidol during the 24 hr recovery period.

Discussion

Results of this study demonstrated that supplemental nitrous oxide does not aggravate PONV after propofol anesthesia for orthognathic surgery even in female and non-smoking patients.

Several reports suggest that some anesthetics such as nitrous oxide and volatile anesthetics, supplemental agents such as opioids, neostigmine, dehydration during anesthesia, female patient, nonsmoking status and a history of PONV or motion sickness are risk factors for PONV.^{7,8} The Consensus Guideline for Managing PONV classified large amount of information into five levels of evidence based on study design (I-V) and three strengths of recommendation based on expert opinion (A-C).⁸

In the guideline, patient-specific risk factors include female sex (IA), nonsmoking status (IV A) and a history of PONV or motion sickness (IV A).⁸ Therefore, only female and nonsmoking patients were selected to avoid sex- and smoking-related errors in the present study. The nasogastric drainage tube itself might cause nausea during the recovery period. In contrast, neostigmine was not administered in all patients because of its emetic action (II A).⁸ All patients received dexamethasone to prevent postoperative edema. Five to 10 mg examethasone has antiemetic effects (II A).⁸ All patient received sufficient fluid transfusion to prevent dehydration (III A)⁸ and

maintained enough hourly urine output. All patients received 3 l/min oxygen via a face mask until 24 hours after extubation (III B).⁸ All patients did not have a history of previous general anesthesia and motion sickness (IV A).⁸ Thus, highly homogeneous character of the patients was assured in the present study.

Total intravenous anesthesia using propofol and fentanyl is sometimes accompanied with blood pressure and heart rate fluctuations during oral and maxillofacial surgery even with an adequate use of local anesthesia. In these situations, supplemental nitrous oxide produces hemodynamic stability along with propofol sparing effects, though nitrous oxide is a well-known emetic agent (II A).⁸ Previous report shows that nitrous oxide and propofol have an additive hypnotic interaction in humans⁹ and also an additive interaction to suppress pressor responses to electrical stimulations of the mental nerve in rabbits.¹⁰

In this study, an addition of nitrous oxide to propofol did not aggravate PONV during the 24 hr recovery period. This result may be attributable to the strong antiemetic effect of propofol.¹⁴ Therefore, supplemental nitrous oxide may be a good candidate to reduce hemodynamic fluctuations without increasing risk of PONV after oral and maxillofacial surgery. This might be partly shown as the smaller propofol infusion rate in the nitrous oxide-propofol group, though not significant. This result is consistent with the results of other investigations reporting that an addition of nitrous oxide to propofol did not increase the risk of PONV after operations other than oral and maxillofacial surgery.¹¹⁻¹³ One study reported that omitting nitrous oxide from general anesthetics decreased PONV when the baseline risk of vomiting was high.¹⁵

Since subjects were female and non-smoking patients in this study, the baseline risk of vomiting was thought to be high. However, patients anesthetized with propofol with or without nitrous oxide showed no difference in PONV scores. This result suggests that propofol could reduce the PONV risk (female, non-smoking, opioid-used) to a significantly lower level.

In this study, operation time in the propofol group was shorter than those in the nitrous oxide-propofol group, though not significant. It is reported that each 30 min increase in the duration of surgery increases PONV risk by 60 %.⁸ However, PONV scores in propofol and nitrous oxide-propofol groups were comparable. Thus, it is suggested that the effect of operation time difference on PONV score should be minimal in this study. Fentanyl dose per body weight in the propofol group was larger than that in the nitrous oxide-propofol group, though not significant. Although fentanyl is also a well-known emetic agent (II A),⁸ it is suggested that the difference in fentanyl dose is negligible when used with propofol.

Since only 28 patients participated in this study, sample size might be small. A power analysis may be appropriate in this situation. However, distribution of PONV scores was same in both groups and only one patient in each group vomited. Therefore, we believe that the effect of supplemental nitrous oxide not to increase the PONV risk after oral and maxillofacial surgery was clearly demonstrated even with relatively small size of samples. Further investigation is warranted to confirm the results of this study in a large population at high PONV risk.

In conclusion, supplemental nitrous oxide does not aggravate PONV after

propofol anesthesia for orthognathic surgery even in female and non-smoking patients.

Nitrous oxide may be a good candidate to reduce hemodymaic fluctuations during propofol anesthesia for orthognathic surgery.

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Table I. Patient characteristics

	Propofol group	Nitrous oxide-propofol group
n	14	14
Age	22.9 ± 5.2	21.8 ± 4.6
Height (cm)	161.7 ± 6.0	161.8 ± 4.4
Body weight (kg)	54.5 ± 8.1	53.3 ± 3.8

Data were shown as mean ± standard deviation.

Table II. Operation time, anesthesia time, emergence time, fluid transfusion, blood loss, urine output, total propofol dose and total fentanyl dose

	Propofol group	Nitrous oxide-propofol group
Operation time (min)	200.9 ± 73.7	246.1 ± 47.4
Anesthesia time (min)	248.9 ± 77.7	296.9 ± 53.3
Emergence time (min)	12.7 ± 6.0	12.2 ± 11.3
Fluid transfusion (ml)	2794.3 ± 641.0	3235.7 ± 878.2
(ml/kg/hr)	12.9 ± 2.9	12.3 ± 2.9
Blood loss (ml)	551.4 ± 223.4	601.3 ± 299.2
Urine output (ml)	702.1 ± 265.2	1019.3 ± 444.2
(ml/kg/hr)	3.2 ± 1.3	3.9 ± 1.6
Total propofol dose (mg)	2037.0 ± 825.0	1860.6 ± 722.6
(mg/kg/hr)	9.4 ± 4.0	7.3 ± 2.5
Total fentanyl dose (mcg)	392.9 ± 78.1	350.0 ± 65.0
(mcg/kg)	7.3 ± 1.7	6.6 ± 1.3

Data were shown as mean ± standard deviation.

Table III. Postoperative nausea and vomiting (PONV) scores

Score	Propofol group	Nitrous oxide-propofol group
0	10	10
1	3	3
2	1	1

Score 0: Patients without PONV throughout the 24 hr recovery period.

Score 1: Patients who had nausea at least one time but no vomiting during the 24 hr recovery period.

Score 2: Patients who had vomiting at least one time during the 24 hr recovery period.