

# The Effect of Nitrous Oxide on the Intraocular Pressure in Patients Undergoing Abdominal Surgery under Sevoflurane and Remifentanil Anesthesia

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## Abstract

**Introduction:** Although inhalational anesthesia and nitrous oxide (N<sub>2</sub>O) are known to affect the intraocular pressure (IOP), little is known about the effect of nitrous oxide on the IOP during sevoflurane and remifentanil anesthesia. In the present study, we examined the effect of balanced anesthesia on the IOP. **Materials and Methods:** After obtaining informed consent, the patients undergoing abdominal surgery under general anesthesia were divided into two groups: N<sub>2</sub>O group (n = 10) and control group (n = 12). General anesthesia was maintained with remifentanil (0.05 - 0.3 µg/kg/min), 33% O<sub>2</sub> and 1.2% sevoflurane to keep ETCO<sub>2</sub> of 35 - 40 mmHg following tracheal intubation. After baseline measurement of IOP (T0, 20 minutes after injection of anesthesia), the patients in the N<sub>2</sub>O group received 67% nitrous oxide, and the patients in the control group received air, with O<sub>2</sub> and 1.2% sevoflurane. Then, IOP was measured at 1 hour (T1), 2 hours (T2), and 3 hours (T3) after anesthesia induction in the supine position. Blood pressure and heart rate were recorded at the same time interval. **Results:** There was no significant difference in the IOP at any period between the two groups. In both groups, the IOP at the T3 was significantly higher than that at T0. **Conclusion:** These results suggest that N<sub>2</sub>O does not affect the IOP in patients undergoing abdominal surgery under sevoflurane and remifentanil anesthesia.

## Keywords

Intraocular Pressure, Nitrous Oxide, Balanced Anesthesia

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## 1. Introduction

Intraocular pressure (IOP) is known to change during perioperative period due to inhalational anesthetic agents like halothane, isoflurane and sevoflurane [1] [2], and opioids such as fentanyl, alfentanil and remifentanil [3]-[7]. Schäfer *et al.* have shown that IOP more reduces during anesthesia with propofol than with sevoflurane, both combined with remifentanil [8].

Although nitrous oxide (N<sub>2</sub>O) may affect IOP [9]-[12], one report indicates that IOP with desflurane and N<sub>2</sub>O does not differ compared with desflurane alone in dogs [11]. Moreover, N<sub>2</sub>O has been shown to have no influence in healthy volunteer [13]. On the other hand, detrimental effect of N<sub>2</sub>O is reported, indicated that the use of N<sub>2</sub>O in patients, who undergo vitreoretinal procedures cause retinal or optic nerve ischemia, results in visual loss [14]-[16].

Sevoflurane combined with remifentanil anesthesia is not known to influence IOP. In addition, it is not well known about the effect of N<sub>2</sub>O on IOP in patients receiving sevoflurane and remifentanil anesthesia in patients with abdominal surgery. Therefore, we examine the effect of N<sub>2</sub>O on the IOP in patients undergoing abdominal surgery under sevoflurane and remifentanil anesthesia.

## 2. Materials and Methods

The study was approved by the Ethics Committee of Akita University Hospital and registered with the UMIN clinical trials registry (ID: UMIN000020241). After obtained informed consent, 22 ASA physical status I or II patients scheduled for elective abdominal surgery were studied. We excluded patients with allergies, unstable angina, congestive heart failure, glaucoma and other ophthalmic disease and past history of eye surgery. The patients were allocated to either of two groups; N<sub>2</sub>O group (n = 10) and control group (n = 12). All patients were premeditated with ranitidine 150 mg 90 min before general anesthesia. Anesthesia was induced with propofol 1 mg/kg, continuous infusion of remifentanil and rocuronium 1mg/kg. The trachea was intubated, and lung ventilation was adjusted to maintain end-tidal CO<sub>2</sub> at 35 - 40 mmHg with 33% oxygen, 1.2% sevoflurane and remifentanil (0.05 - 0.3 µg/kg/min). The patients in the N<sub>2</sub>O group received 33% oxygen and 67% N<sub>2</sub>O, and the patients in the control group received air instead of oxygen and N<sub>2</sub>O. IOP was measured at 20 min after induction of anesthesia (T0), 1 hour after T0 (T1), 2 hours after T0 (T2), and 3 hours after T0 (T3) at the supine position using PT100 portable non-contact tonometer (Reichert, INC, Depew, NY, USA). Blood pressure and heart rate were recorded at the same time interval. We measured the IOP three times in each epoch, and then calculated the mean value.

We defined hypotension as a SBP (systolic blood pressure) ≤ 80% of the preinduction baseline SBP, hypertension as a SBP > 140% of the preinduction baseline SBP, and bradycardia as HR < 40 bpm. Hypotension was treated with an intravenous bolus of phenylephrine 50 µg or ephedrine 5 mg and bradycardia was treated with an intravenous bolus of atropine 0.5 mg.

Data were expressed as mean ± SD. Student t-test was used to compare the data between two groups, and analysis of variance for repeated measures was performed to access differences within the groups. *P* < 0.05 was considered as statistically significant.

## 3. Results

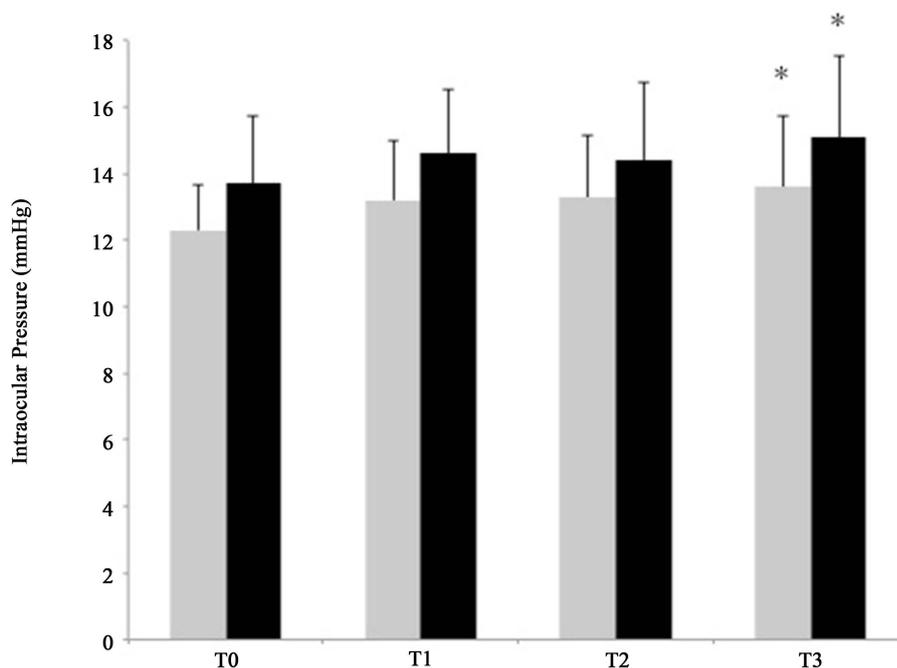
The patients in the two groups were comparable with regards to demographic and hemodynamic data (Table 1 and Table 2).

Although there were no significant differences between the two groups in IOP at any measuring points, IOP at T3 was significantly higher than that at T0 in both groups (Figure 1).

**Table 1.** Patients' demographic data.

	N <sub>2</sub> O group	Control group	<i>P</i> value
Age (years)	59 ± 12	55 ± 15	0.64
Gender (male/femal)	4/6	3/9	0.65
Height (cm)	157 ± 13	159 ± 12	0.63
Weight (kg)	56 ± 14	58 ± 12	0.65
ASA (grade1/2)	4/6	3/9	0.65

Values are mean ± SD or numbers. No significant difference.



**Figure 1.** Changes of the intraocular pressure (IOP) during study period. IOP did not differ between the N<sub>2</sub>O groups (gray bar) and the control group (black bar) at any measuring points. IOP values at T3 in both groups were higher than those at T0. T0 = 20 min after induction of anesthesia, T1 = 1 hour after T0, T2 = 2 hours after T0, T3 = 3 hours after T0. Values were mean ± SD. \**P* < 0.05 versus T0.

**Table 2.** Changes of intraocular pressure.

	Group	T0	T1	T2	T3	<i>P</i> value
Mean Blood Pressure (mmHg)	N <sub>2</sub> O group	69 ± 11	68 ± 9	68 ± 8	69 ± 10	0.84
	Control group	70 ± 14	73 ± 10	67 ± 7	72 ± 11	
Heart Rate (beats/min)	N <sub>2</sub> O group	71 ± 8	69 ± 10	68 ± 13	69 ± 11	0.09
	Control group	64 ± 11	63 ± 12	62 ± 10	67 ± 9	
ETCO <sub>2</sub> (mmHg)	N <sub>2</sub> O group	36 ± 0.8	36 ± 0.9	36 ± 0.8	37 ± 1.4	0.13
	Control group	35 ± 0.4	36 ± 0.9	36 ± 0.9	36 ± 1.2	

T0 = 20 minutes after induction, T1 = 1 hour after T0, T2 = 2 hour after T0, T3 = 3 hour after T0. Values = mean ± SD. There were no significant different between two groups.

There was no patient who developed hypertension, hypotension and bradycardia during the study period.

#### 4. Discussion

We conducted a prospective, randomized study to evaluate the effects of N<sub>2</sub>O on IOP during sevoflurane and remifentanyl anesthesia. Our results demonstrated that N<sub>2</sub>O did not affect IOP during 3 hours in patients under general anesthesia with sevoflurane and remifentanyl. However, IOP increased at 3 hours after induction of anesthesia compared with starting point in both patients with and without N<sub>2</sub>O.

Intraocular pressure (IOP) is known to changing at perioperative period due to anesthetic maneuvers [3] [17], anesthetic agents [4] [18]-[21], and patient's position [22]-[27] and hemodynamics [28]. Tracheal intubation [29], succinylcholine [5]-[7], inhalational anesthesia [1] [2] [8], and nitrous oxide (N<sub>2</sub>O) [21] may influence IOP. Inhalational anesthetics and propofol have been shown to decrease IOP [8], whereas succinylcholine can increase IOP [5]-[7]. Previous studies demonstrated that general anesthesia with halothane, enflurane, propofol,

and fentanyl would decrease IOP after tracheal intubation [2]-[5]. These range of reduction varied with type of anesthesia. Tracheal intubation could lead to elevate IOP [17], however, this effect can be minimized by various method [5]-[7]. In this study, we did not measure IOP before anesthesia. Therefore, we could not compare the IOP values between before and after tracheal intubation. Moreover, none of the previous reports that showing the changes of the IOP during sevoflurane and remifentanyl anesthesia in patients undergoing abdominal surgery was existed.

Although major determinants for IOP include the production rate of aqueous humor, vitreous volume, sclera rigidity, choroidal blood volume, and orbicularis oculi muscle tension [12], there have been few studies to assess the effect of nitrous oxide on IOP [10]-[13]. Lalwani *et al.* have shown that nitrous oxide inhalation did not significantly change IOP from baseline values in a population of healthy adults [13]. Our result of present study was consistent with their result.

IOP at T3 in both groups were significant greater than IOP at T0 in this study. Because hemodynamics and anesthesia was similar during the study period, the possibility of blood pressure and anesthesia can be excluded. However, it remains unknown what was the effect of IOP at T3. IOP at T3 in both group were within normal range and did not differ between the two groups. Therefore, it is clear that N<sub>2</sub>O does not affect the elevation of IOP at T3.

Based on the present and previous similar study [11]-[13], the effect of N<sub>2</sub>O would not affect the IOP during 3 hours sevoflurane and remifentanyl anesthesia in patients undergoing abdominal surgery. Our study had the following possible limitations. We had recruited the small number of patients with ASA physical status I or II. It remains unknown if the results will be applicable to other populations such as patients with glaucoma, under head down position surgery or laparoscopy. The difference of the IOP before and after sevoflurane and remifentanyl anesthesia was not clear from this study and warranted the additional studies. Future studies will be needed to clarify the effects of N<sub>2</sub>O long exposure on IOP in other patient populations and surgery.

## 5. Conclusion

In conclusion, N<sub>2</sub>O did not affect IOP during abdominal surgery under sevoflurane and remifentanyl anesthesia. With or without N<sub>2</sub>O, IOP at 3 hours after induction of anesthesia was significantly higher than that at 20 minutes after (T0).

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## Competing Interest

The authors have no conflicts of interest to declare, financial or otherwise.

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