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Utility and safety of low-concentration nitrous oxide anesthesia in ptosis surgery

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Abstract

To evaluate the utility of low-concentration nitrous oxide (N_2O) anesthesia in ptosis surgery

This study was a retrospective consecutive case series that included 54 successive patients with blepharoptosis who underwent bilateral levator aponeurosis advancement and on whom skin resection performed by the same surgeon between August 2016 and July 2017. Among these patients, 27 were operated with a local anesthesia injection (air group) and 27 with a local anesthesia injection and low-concentration N_2O anesthesia (N_2O group). All N_2O cases used a total of 6 L of gas comprising 70% oxygen and 30% N_2O. Preoperative and postoperative blood pressure (BP) and heart rate (HR) and intraoperative pain, anxiety, nausea, and memory were measured immediately after surgery using visual analog scale score (VASS). Additionally, perioperative side effects were examined.

There was no significant difference in age, sex, and preoperative and postoperative margin reflex distance (MRD) between the 2 groups (all $P > .05$). The intraoperative mean peripheral oxygen saturation was significantly higher (97.5% ± 1.6% vs 99.5% ± .6%, $P < .001$), intraoperative HR was significantly lower (78.2 ± 12.8 vs 70.7 ± 11.6 bpm, $P = .02$), and operation time was significantly shorter (33.1 ± 8.1 vs 29.4 ± 10.3 minutes, $P = .03$) in the N_2O group than in the air group.

Difference between intraoperative and preoperative systolic BP (BPs) (+15.8 ± 18.0 vs +3.1 ± 21.7 mm Hg, $P = .02$), diastolic BP (BPd) (+7.0 ± 17.4 vs −2.3 ± 13.6 mm Hg, $P = .04$), and HR (3.2 ± 8.5 vs −3.9 ± 9.4 bpm, $P = .01$) was significantly lower in the N_2O group than in the air group.

VASS of intraoperative pain was significantly lower in the N_2O group than in the air group (49.5 ± 24.7 vs 22.6 ± 14.9, $P < .001$), whereas intraoperative anxiety and memory did not present significant differences between the groups ($P = .09$ and $P = .45$, respectively). Intraoperative nausea score was 0 for all cases in both groups. There was no other side effect.

Ptosis surgery with anesthesia using 30% N_2O may effectively suppress intraoperative BP and HR along with pain and shorten the operation time without side effects such as nausea.

Abbreviations: BP = blood pressure, HR = heart rate, MRD = margin reflex distance, N_2O = nitrous oxide, PSA = procedural sedation and analgesia, SpO_2 = mean peripheral oxygen saturation, VASS = visual analog scale score.

Keywords: blepharoplasty, nitrous oxide anesthesia, procedural sedation and analgesia, ptosis

1. Introduction

Anesthesia is essential for surgery. It is impossible to perform all ophthalmic operations with local anesthesia; it is not unusual to experience difficulties when performing operations with local anesthesia. According to a 2017 report by Eke et al, 4.1% of 375,000 cataract surgeries in the United Kingdom were performed under general anesthesia, whereas 92% were performed with local anesthesia only and 3.9% used local anesthesia with sedation.[1] Even if local anesthesia suppresses the pain caused by the operation to a certain degree, distress such as anxiety of the patient still remains.

Procedural sedation and analgesia (PSA) refers to the use of sedatives and analgesics when patients complain of strong anxiety and pain during operations and treatments. There are reports of serious conditions such as hypotension and respiratory depression during PSA with intravenous anesthetic performed by paramedics[2–4]; thus, PSA is challenging for ophthalmologists who are not familiar with general care. Studies on the relationship between self-efficacy and pain showed that a high level of self-efficacy was related to high pain tolerance, wherein if patients are experiencing anxiety, the same level of pain stimulus can cause more pain.[5–8]

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Laughing gas (nitrous oxide; N_2O) was discovered by a British chemist Joseph Priestley in 1772. A dentist, Horace Wells, inhaled N_2O gas to extract his own wisdom tooth in 1844, which is said to be the first medical use of N_2O gas anesthesia. The blood/gas partition coefficient of N_2O is .47, and the minimum alveolar concentration is 105, which means that induction of and emergence from anesthesia are quite fast.[9,10] However, its unconsciousness-inducing action is extremely mild. Its analgesic and anti-anxiety effects are strong, but there is no muscle relaxation, respiratory depressant, or blood pressure (BP)-lowering effect. Reportedly, the analgesic effect of 20% N_2O gas anesthesia is equivalent to 15 mg of morphine.[11] It could provide additional analgesia, anti-anxiety effect, and respiratory control to local anesthesia without risks such as fluctuating BP. The clinical safety of N_2O gas anesthesia is well known, and the utility and safety of its combined use in local anesthesia such as PSA are being recognized in dentistry, emergency medicine, and obstetrics and gynecology.[12,13] The combined use of N_2O gas anesthesia with local anesthesia in ophthalmic operations may be useful, but there is no report discussing the utility of low-concentration N_2O anesthesia in the field of ophthalmology.

The solubility of N_2O gas in the blood is low (blood/gas partition coefficient = .47); thus, it acts extremely fast in the brain (30–60 seconds) and its clearance from the lung is also extremely fast. Anesthesia is induced within few minutes, and the patient can emerge in few minutes.[14]

This study aimed to compare changes in vital signs, pain, anxiety, and memory during surgery for patients with blepharoptosis who underwent blepharoplasty using local anesthesia injection with those who underwent blepharoplasty using same local anesthesia injection combined with low-concentration N_2O anesthesia.

2. Methods

This study was approved by the ethics committee and adhered to the principles of the Declaration of Helsinki and was a retrospective consecutive case series performed at the Department of Ophthalmology of Saneikai Tsukazaki Hospital, Japan, between August 2016 and July 2017. All patients provided written informed consent. Patients with bilateral blepharoptosis who underwent bilateral levator aponeurosis advancement and skin resection between August 2016 and July 2017 were enrolled. From August 2016, 27 successive patients (54 eyes; age, 73.26 ± 10.55 years; 17 males) were operated on with local anesthesia injection and room air without N_2O gas anesthesia (air group). In January 2017, the use of N_2O gas anesthesia became possible in the hospital, 27 successive patients (54 eyes; age, 74.74 ± 7.45 years; 12 males) were operated on with the same local anesthesia injection and 6 L of low-concentration N_2O gas anesthesia (70% oxygen and 30% N_2O; N_2O group). The N_2O group was induced with N_2O gas anesthesia from the moment patient sat down in the operation chair until the end of the operation. Preoperative margin reflex distance (MRD) of the air and N_2O gas groups was 1.32 ± 1.03, (mean ± standard deviation) and 1.77 ± .90 mm, respectively; there was no difference between both groups ($P = .10$). The exclusion criteria were undergoing another eye operation and the presence of eye or systematic disease.

All operations were performed by the same well-experienced ophthalmologist. For all cases, intraoperative local anesthesia was induced using 3 ml of lidocaine with 2% epinephrine per eyelid. All cases received levator aponeurosis advancement, which was sutured to the tarsus. Patients were requested to open and close their eyes, and the postoperative MRD (mm) was targeted to 3 to 3.5 mm during the operation. We used Psychorich T-70 (SEKIMURA) and IS cannula (SEKIMURA) for N_2O gas anesthesia (Fig. 1). Preoperative systolic BP (BPs, mmHg), diastolic BP (BPd, mmHg), heart rate (HR, bpm), and intraoperative mean BPs, as well as mean BPd, and mean peripheral oxygen saturation (SpO_2, %) were examined. Intraoperative pain, anxiety, memory, and nausea were examined using the 10-cm visual analog scale score (VASS)[15] immediately after surgery. Preoperative BP and HR were measured once using a BP cuff. Intraoperative SpO_2, BP, and HR were measured using a pulse oximeter attached on the index finger, BP cuff, and two-lead electrocardiogram, respectively, every 5 minutes until the end of operation. As changes in vital signs, intraoperative mean BPs − preoperative BPs, intraoperative mean BPd − preoperative BPd, and intraoperative mean HR − preoperative HR were examined. To evaluate ptosis surgery, MRD was measured preoperatively and 3 months postoperatively.

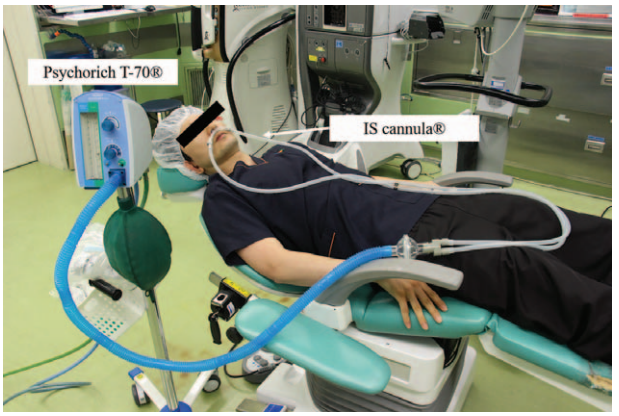

Figure 1. Psychorich T-70 (SEKIMURA) and IS cannula (SEKIMURA) for N_2O anesthesia (the photograph will be replaced). A designated cannula is attached to the patients nose from the anesthesia machine for inhalation. An intravenous line is not required.

Statistical analysis was performed using Shapiro–Wilk test and O'Brien test of homogeneity of variance. When the results indicated normal distribution and equal variance, the Student *t* test was performed. When the results indicated nonnormal distribution, the Mann–Whitney *U* test was performed. We performed Student *t* test for BP and HR and Mann–Whitney *U* test for age, operation time, VASS score, SPO_2, (intraoperative − preoperative) BPs, (intraoperative − preoperative) BPd, and (intraoperative − preoperative) HR. We used Chi-Squared test for sex-based differences. Significance level was $P < .05$; statistical analysis was performed using JMP 14.3 (SAS Inc., Cary, NC, USA).

3. Results

In all cases, operations were performed without any problems, and there were no notable complications. There was no significant difference in age or sex between the groups ($P = .99$ and $P = .17$, respectively). The operation time was significantly shorter in the N_2O group than in the air group (33.1 ± 8.1 vs 29.4 ± 10.3 minutes, $P = .03$). There was no abnormality in measured vital signs that would require treatment. Although there was no difference in preoperative BPs, BPd, and HR between the 2 groups ($P > .05$), the intraoperative HR was significantly lower in

Table 1

Patient background of the air group and the N_2O group.

	Air		N_2O		
	Mean	SD	Mean	SD	*P*
N	27		27		
Age (years)	73.26	10.55	74.74	7.45	.55
Time (min)	33.07	8.13	29.37	10.27	.03*
Preoperative BPs (mmHg)	131.44 (88–166)	20.75	138.56 (98–180)	21.01	.22
Preoperative BPd (mmHg)	66.85 (38–96)	15.79	73.19 (48–108)	13.48	.12
Preoperative HR (bpm)	75.89 (61–98)	10.1	74.63 (48–108)	11.2	.67
Intraoperative BPs (mmHg)	147.19 (107.71–176.5)	17.59	141.64 (118.83–181)	18.25	.26
Intraoperative BPd (mmHg)	73.8 (56.5–102)	9.81	70.91 (45–91.83)	12.21	.34
Intraoperative HR (bpm)	78.19 (57.4–116.17)	12.75	70.71 (52.25–99.17)	11.62	.02†
Intraoperative SPO2 (%)	97.48	1.55	99.5	.64	<.001*
Preoperative R MRD (mm)	.64 (−3.0~2.0)	1.19	.93 (−1.0~2.5)	1	.67
Postoperative L MRD (mm)	1.06 (−2.0~2.5)	1.03	.73 (−2.0~2.5)	1.01	.15
Postoperative R MRD (mm)	3.22 (2.5~3.5)	.37	3.38 (2.5~3.5)	.19	.07
Postoperative L MRD (mm)	3.3 (2.5~3.5)	.33	3.38 (3.0~3.5)	.19	.41

There was no difference in age between the groups. There was no difference in preoperative BP and HR between the groups ($P > .05$). There was a significant difference in operation time, intraoperative HR, and SpO_2 between the groups ($P < .05$).

* Mann–Whitney *U* test $P < .05$.

† Student *t* test $P < .05$.

BP = blood pressure, HR = heart rate, MRD = margin reflex distance, N_2O = nitrous oxide, PSA = procedural sedation and analgesia, SD = standard deviation, SpO_2 = mean peripheral oxygen saturation.

the N_2O group than in the air group (70.7 ± 11.6 vs 78.2 ± 12.8 bpm, $P = .02$). The intraoperative SpO_2 was significantly higher in the N_2O group than in the air group (99.5 ± .64% vs 97.5 ± 1.6%, $P < .001$) (Table 1). Changes in vital signs from preoperative to intraoperative were as follows: intraoperative BPs − preoperative BPs was +15.8 ± 18.0 mm Hg in the air group and +3.1 ± 21.7 mm Hg in the N_2O group; the amount of increase was less in the N_2O group ($P = .02$). Intraoperative BPd − preoperative BPd was +7.0 ± 17.4 mm Hg in the air group and −2.3 ± 13.6 mm Hg in the N_2O group; there was significantly less increase in the N_2O group ($P = .03$). Similarly, intraoperative HR − preoperative HR was +3.2 ± 8.5 bpm in the air group and −3.9 ± 9.4 bpm in the N_2O group; there was significantly less increase in the N_2O group ($P = .01$) (Fig. 2). VASS showed that intraoperative pain was 49.5 ± 24.7 in the air group and 22.6 ± 14.9 in the N_2O group; the score was significantly lower in the N_2O group than in the air group ($P < .001$). Intraoperative anxiety was 33.9 ± 29.1 in the air group and 21.6 ± 21.5 in the N_2O group; the mean was lower in the N_2O group than in the air group, although the difference was not statistically significant ($P = .09$). Intraoperative memory was 93.1 ± 14.0 and 87.2 ± 24.2 without no significant difference, indicating that memory was maintained in both groups ($P = .45$). Intraoperative nausea was 0 in all cases in both groups, that is, no patient experienced nausea (Fig. 3). There was no drop in BP, respiratory depression, or nausea in either group. All patients were able to walk back to the

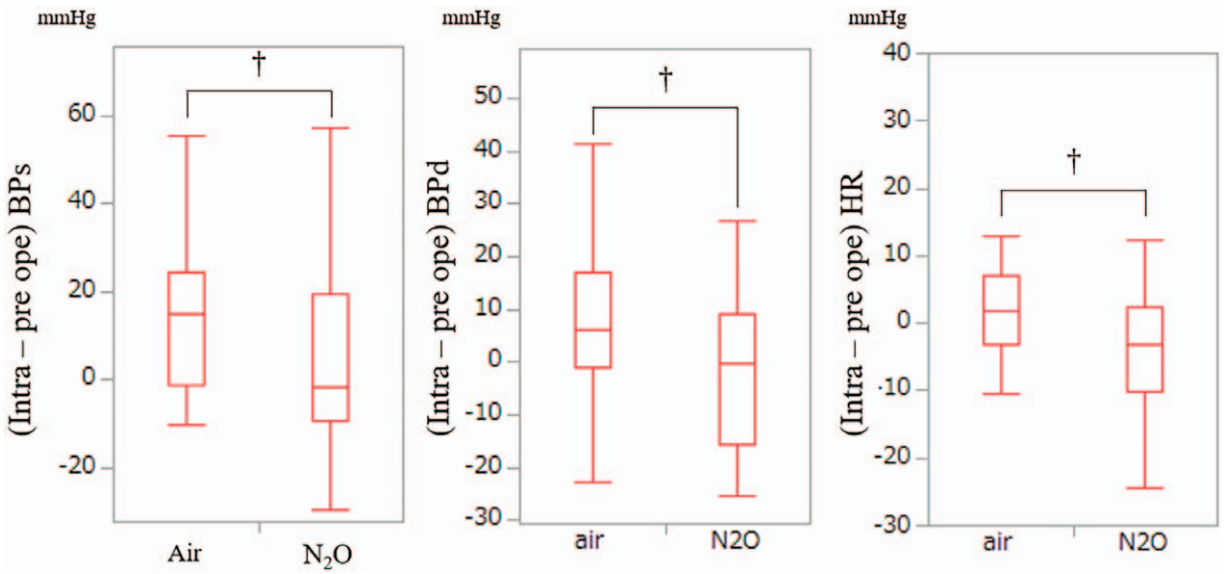

Figure 2. Difference in the preoperative and postoperative BP and HR. Differences between preoperative and postoperative BPs, BPd, and HR were significantly less in the N_2O group than in the air group. Compared with preoperative values, values increased during the operation in the air group but decreased in the N_2O group. †Student *t* test $P < .05$.

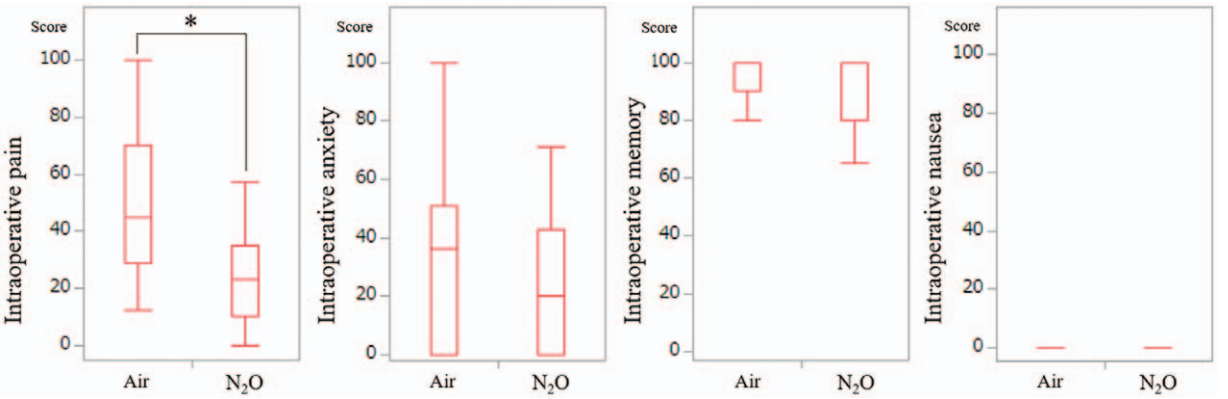

Figure 3. Intraoperative pain, anxiety, memory, and nausea scores. VASS examination showed that intraoperative pain was significantly lower in the N_2O group than in the air group ($P < .001$). There was no nausea in either group. Intraoperative memory score was high in both groups, and there was no anesthesia amnesia. *Mann–Whitney U test $p < .05$.

outpatient department immediately after anesthesia and could head home after 30 minutes of observation. In addition, there was no adverse event that could be considered a side effect during or after operation. Intraoperative and postoperative bilateral MRD did not show statistically significant difference between the groups (right eye MRD, $P = .07$; left eye MRD, $P = .41$). Thus, the use of N_2O did not have an impact on the opening of the eye postoperatively (Table 1).

4. Discussion

Ptosis surgery with low-concentration N_2O gas anesthesia significantly suppressed BPs, BPd, and HR. The VASS questionnaire at the end of the operation showed that intraoperative pain was sufficiently minimized ($P < .001$). The mean intraoperative anxiety of the N_2O group was lower than that of the air group, with no statistically significant difference. There was no nausea or abnormal vital signs during the operation or no side effect.

There was no significant difference in preoperative and postoperative MRD in either group, and N_2O gas anesthesia did not have much impact on intraoperative quantification and postoperative MRD for blepharoplasty.

Usually, BP and HR tend to increase during the operation than before the operation because of the tension of undergoing operation, pain of the local anesthesia injection at the beginning of the operation, and pain during the operation. In fact, in the air group, BP and HR increased during the operation; however, in the N_2O group, increase in BP and HR during the operation was significantly suppressed because intraoperative pain and tension were reduced using N_2O gas anesthesia.

Furthermore, no clear drop in BP, bad mood, or respiratory depression that would indicate a side effect of N_2O gas anesthesia was noted. Intraoperative SpO_2 was significantly higher in the N_2O group than in the air group, but this was likely because of N_2O gas anesthesia being supplied with oxygen.

Intravenous anesthesia with propofol, opioids, and benzodiazepines causes hypotension and/or respiratory depression, making management of vital signs difficult. In addition, its sedative action is strong and the recovery time following the anesthesia is long. Oral analgesics such as nonsteroidal anti-inflammatory drugs are easy to use, but their analgesic effect is insufficient.[2–4] In contrast, N_2O has strong analgesic and anti-anxiety effects with mild sedative and hypnotic effects and little impact on circulatory and respiratory systems; thus, the risk for hypotension or respiratory depression is extremely limited. Additionally, it does not require an intravenous (IV) line and patients only need to inhale; thus, burden on patients and healthcare providers is extremely limited.[12,13] The blood/gas partition coefficient is small, and as it quickly moves from the alveoli to the blood, its effect is fast and emergence from anesthesia is also fast.[9,10]

In the past, ophthalmic operations with local anesthesia only managed pain with local injection such as lidocaine and did not control anxiety and additional pain caused by the operation. Although PSA was too challenging for ophthalmologists, with low-concentration N_2O anesthesia, the risk of complications such as changes in vital signs and respiratory depression is extremely low and ophthalmologists without anesthetic expertise can easily introduce it. It could be a blessing not only for patients who have been suffering through ophthalmic operations with local anesthesia but also for ophthalmologists who will be able to perform even safer operations. However, there are disadvantages with N_2O. Because it tends to escape to dead space, when high-concentration N_2O was used as a general anesthetic for a patient with a vitreous cavity filled with gas, ocular pressure increased and caused ophthalmic artery occlusion.[16] However, no examination has been performed regarding low concentration, spontaneous respiration, and the use of a cannula as done in this study. Specifically, in the field of ophthalmology, a case of a complication with increased ocular pressure caused by a general anesthetic has been reported[16]; it has hardly ever been used in recent years. However, it could be extremely useful if cases and usages are carefully examined.

The operation time was 3 minutes shorter than the average in the N_2O group than in the air group. All operations were performed by the same ophthalmologist; thus, this difference might have been caused by ease of operation in the N_2O group due to patients straining less, difference in movements, and difference in intraoperative bleeding. However, we did not examine these factors in this study.

This study was a retrospective and not a prospective intervention study. Therefore, classification of both groups and patient backgrounds might have had an impact.

5. Conclusions

N_2O anesthesia does not require an intravenous line and is easy to use because it only requires a nasal cannula. Moreover, it exerts little burden on nurses and patients. Low-concentration N_2O gas anesthesia has no side effects; its intraoperative management is similar to that of conventional local anesthesia. It is quite safe to perform for ophthalmologists and could be a useful tool to manage intraoperative pain and vital signs.

Author contributions

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Validation: Santaro Noguchi.
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