

Diffusion of nitrous oxide through endotracheal tube cuffs.

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Abstract

During general anesthesia using nitrous oxide (N₂O), N₂O diffuses into the tracheal tube cuff and increases cuff pressure, potentially causing tissue damage in the trachea. However, the permeability of the tube cuff to N₂O flowing into the cuff is unknown. Here, we examined decrease in cuff pressure and N₂O permeability of the tracheal tube cuff. Two tracheal tubes, i.e., Portex Blue Line Profile, Soft-Seal Cuff (SPN) and Mallinckrodt Nasal RAE Tracheal Tube Cuffed, Murphy Eye (MRN), were examined. Six gas samples (air, oxygen, 70% N₂O in oxygen, 50% N₂O in oxygen, 30% N₂O in oxygen, and a mixture of 60% N₂O in oxygen to air [4:3]) were prepared and used to inflate both cuffs at a pressure of 30 cmH₂O. Cuff pressures were recorded at every 5 min. After inflation with air, cuff pressures reached 26.8 ± 1.9 and 30.0 cmH₂O for MRN and SPN, respectively, within 60 min. Inflation with 70% N₂O dramatically decreased cuff pressures (3.2 ± 0.4 and 5.2 ± 1.1 cmH₂O, respectively). The rate of pressure decrease was dependent on the concentration of N₂O and was more rapid for MRN than SPN. Inflation with the mixture gas decreased the pressure to 14.8 ± 2.7 and 17.4 ± 3.8 cmH₂O for MRN and SPN, respectively, within 60 min. Here, we provided the first analysis of deflating cuff pressures, which may help to predict patterns for cuff pressure deflation in clinical practice. This study model may be beneficial for the study of ventilator-associated pneumonia.

Keywords: Nitrous oxide, Endotracheal tubes, Diffusion

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Introduction

Nitrous oxide (N₂O) is an inhalational anesthetic that is frequently used for general anesthesia. While N₂O is not sufficient for maintaining general anesthesia if used alone, when used in combination with a volatile inhalation agent, N₂O decreases the minimum alveolar concentration (MAC) of the volatile inhalational agent, thereby reducing the amount of the agent required during longer procedures [1]. However, N₂O increases the intracuff pressure of the tracheal tube due to diffusion of N₂O into the cuff during general anesthesia [2]. Intracuff pressure increases steadily and reaches a level high enough to impede the microcirculation in the tracheal mucosa within 1 h [3,4], which may cause damage to the tracheal tissue. This represents a major complication of N₂O use.

In anesthesia using N₂O, it is thought that the N₂O concentration in the tube cuff is close to the N₂O concentration prescribed for the patient. Usually, at the end

surgery, administration of N₂O is stopped, and the patient is given 100% oxygen or air. Subsequently, the patient recovers from anesthesia and is moved to the intensive care unit. In such cases, the N₂O that flowed into the cuff will be transferred to outside of the cuff, which may cause a decrease in cuff pressure. This decrease in cuff pressure may then trigger ventilator-associated pneumonia (VAP) [5]. However, few studies have examined the decrease in cuff pressure associated with N₂O administration. Therefore, in this study, we examined the decrease in cuff pressure caused by the flow of N₂O into the cuff.

Materials and Methods

Tracheal tubes

The Portex Blue Line Profile, Soft-Seal Cuff (SPN) tube and Mallinckrodt Nasal RAE Tracheal Tube Cuffed, Murphy Eye (MRN) tube were used as test tracheal tubes in this study. The MRN tube was equipped with a normal

polyvinyl cuff. Cuff filling volumes to achieve 30 cmH₂O cuff pressure were 15.5 and 14 ml of air for SPN and MRN, respectively.

Measurement procedures

Six gas preparations (air, oxygen, 70% N₂O in oxygen, 50% N₂O in oxygen, 30% N₂O in oxygen, and TGM [a three-gas mixture of 60% N₂O in oxygen to air at a 4:3 ratio]) were analyzed (Table 1). SPN and MRN were inflated with the various gases under temperature conditions of 23°C. Initially, the cuff pressure was adjusted to 30 cmH₂O by using cuff pressure manometers (VBM Cuff Controller Inflator from Smiths Medical) and was measured and recorded every 5 min for 60 min thereafter. These measurements were repeated five times for each group. All pressure measurements are presented in cmH₂O.

Statistical analysis

Statistical analysis was performed on a personal computer

Table 1: Compositions of gases in the six gas groups.

Groups	Composition
Air	78% nitrogen/ 22% oxygen (Air)
Oxygen	100% oxygen
70% N ₂ O	70% nitrous oxide/ 30% oxygen
50% N ₂ O	50% nitrous oxide/ 50% oxygen
30% N ₂ O	30% nitrous oxide/ 70% oxygen
TGM	25.7% nitrous oxide/ 29.7% oxygen/ 44.6% nitrogen

Table 2: Changes in intracuff pressure for MRN for the five gas groups every 5 min for 60 min. The air group is the control group. Data is expressed as mean ± SD. *P<0.05 versus the air group (Dunnett's t-test; N = 5 for each group).

	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min
Air	29.6 ± 0.89	29.4 ± 0.89	28.6 ± 1.14	28.6 ± 1.14	28.4 ± 1.51	28.0 ± 1.58	28.0 ± 1.58	27.8 ± 1.64	27.2 ± 1.78	27.0 ± 2.12	26.8 ± 1.92	26.8 ± 1.92
oxygen	29.8 ± 0.44	29.6 ± 0.54	29.0 ± 0.70	28.0 ± 0.70	27.8 ± 1.09	27.0 ± 1.22	25.8 ± 1.09	24.4 ± 1.14*	23.6 ± 0.89*	23.0 ± 0.70*	22.2 ± 1.48*	22.2 ± 1.48*
70% N ₂ O	23.6 ± 3.78*	17.0 ± 1.87*	12.8 ± 1.48*	9.40 ± 0.89*	7.40 ± 0.89*	5.80 ± 0.83*	5.20 ± 0.83*	4.40 ± 0.54*	4.00 ± 0.70*	3.60 ± 0.54*	3.40 ± 0.54*	3.20 ± 0.44*
50% N ₂ O	24.2 ± 2.04*	19.0 ± 2.34*	16.4 ± 1.81*	13.0 ± 1.87*	11.0 ± 1.58*	9.20 ± 1.30*	8.00 ± 1.00	6.80 ± 0.83*	5.60 ± 0.54*	5.20 ± 0.44*	4.80 ± 0.44*	4.40 ± 0.54*
30% N ₂ O	27.4 ± 1.14	24.4 ± 1.67*	21.4 ± 1.94*	18.8 ± 1.30*	17.2 ± 1.64*	15.2 ± 1.30*	13.4 ± 1.14*	12.0 ± 1.22*	10.4 ± 0.89*	9.20 ± 0.44*	8.20 ± 0.44*	7.20 ± 0.44*

Table 3. Changes in intracuff pressure for SPN for the five gas groups every 5 min for 60 min. The air group is the control group. Data is expressed as mean ± SD. *P<0.05 versus the air group (Dunnett's t-test; N = 5 for each group).

	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min
air	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00	30.0 ± 0.00
oxygen	30.0 ± 0.00	29.8 ± 0.44	29.4 ± 0.89	29.4 ± 0.89	29.4 ± 0.89	29.0 ± 1.22	28.6 ± 1.51	28.0 ± 2.82	27.4 ± 2.50*	27.2 ± 2.48*	27.2 ± 2.48*	27.0 ± 2.34*
70%N ₂ O	27.8 ± 0.83	23.8 ± 0.83*	21.2 ± 1.30*	19.0 ± 1.00*	16.4 ± 1.14*	13.8 ± 1.09*	11.4 ± 1.14*	9.80 ± 0.83*	8.00 ± 0.70*	6.80 ± 0.83*	6.20 ± 0.83*	5.20 ± 1.09*
50%N ₂ O	27.2 ± 0.83	24.0 ± 1.58*	21.8 ± 0.83*	20.0 ± 1.00*	18.4 ± 1.34*	17 ± 1.41	15.6 ± 1.51*	14 ± 1.41*	12.6 ± 1.34*	11.2 ± 0.83*	10.2 ± 0.83*	9.20 ± 0.83*
30%N ₂ O	28.2 ± 0.44	26.6 ± 0.89*	25.2 ± 1.30*	23.6 ± 1.81*	22.8 ± 1.78*	21.8 ± 1.78*	20.8 ± 2.04*	20.0 ± 1.87*	19.0 ± 2.34*	18.0 ± 2.34*	17.6 ± 2.60*	17.0 ± 2.34*

by using SPSS 16.0 (SPSS Japan Inc., Japan) and Ekuseru-Toukei 2006 software (Social Survey Research Information Co. Ltd., Japan). All results are expressed as mean ± SD (SD). Homoscedasticity was tested using the Bartlett's test. One-way repeated measures analysis of variance (ANOVA) was used for comparison of cuff pressures between the five gas groups (i.e., excluding the TGM group) followed by Dunnett's test for multiple comparisons. In addition, Student's t-tests were used for comparison of cuff pressures between the air and TGM groups. A probability of less than 0.05 was considered significant. Approximations were used to determine changing cuff pressures in each gas group.

Results

Tables 2 and 3 shows mean changes in cuff pressures for MRN and SPN over time for the five gas groups (air, oxygen, 70% N₂O, 50% N₂O, and 30% N₂O), and Figures 1 and 2 show deflation responses of MRN and SPN cuff pressures. In comparison with the air group, the oxygen group showed gradually decreasing cuff pressures, reaching significance at 40 min. Additionally, in the N₂O groups, cuff pressures decreased more rapidly than in the oxygen group, with the rate of decrease being dependent on the concentration of N₂O. In the 70% N₂O group, cuff pressures changed more dramatically than those in the 50% and 30% N₂O groups. Significant decreases were observed after only 10 or 20 min for MRN and SPN, respectively. By 60 min, cuff pressures in the 70% N₂O group were 3.20 ± 0.44 and 5.20 ± 1.09 cmH₂O for MRN and SPN, respectively, as compared with

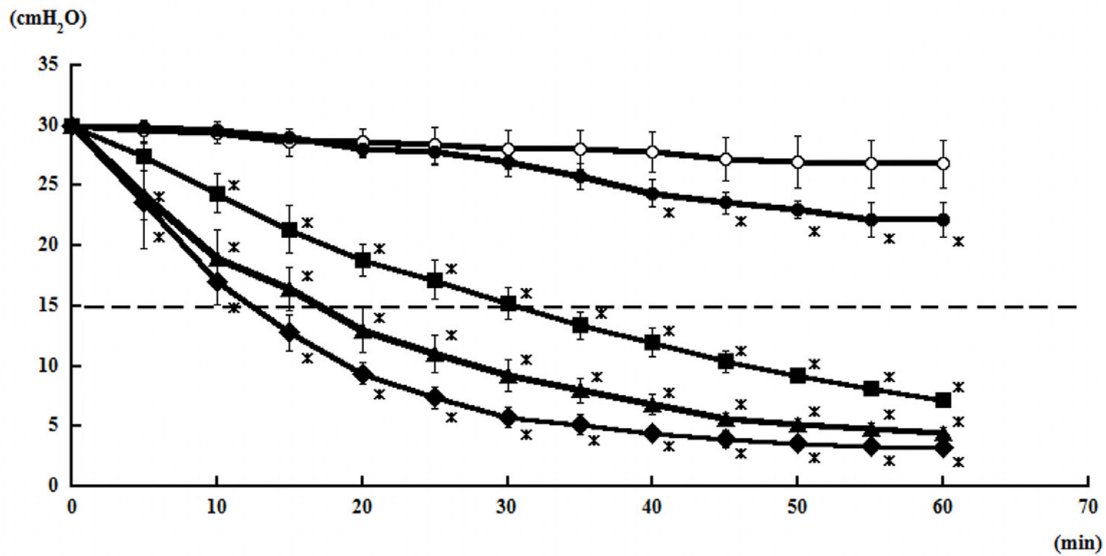


Figure 1. Changes in the MRN cuff pressure over time. Changes were measured every 5 min for 60 min in the five gas groups. Data is expressed as mean \pm SD. Open circles represent the air group (control). Solid circles represent the oxygen group. Squares represent the 30% N_2O group. Triangles represent the 50% N_2O group. Diamonds represent the 70% N_2O group. * $P < 0.05$ versus the air group (Dunnett's t -test; $N = 5$ for each group).

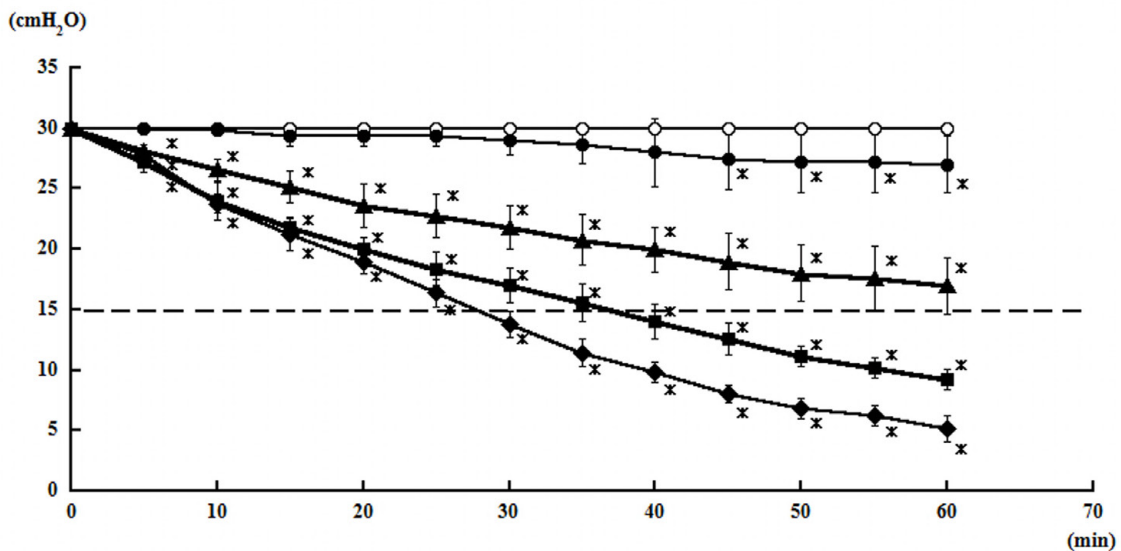


Figure 2. Changes in the SPN cuff pressure over time. Changes were measured every 5 min for 60 min in the five gas groups. Data is expressed as mean \pm SD. Open circles represent the air group (control). Solid circles represent the oxygen group. Squares represent the 30% N_2O group. Triangles represent the 50% N_2O group. Diamonds represent the 70% N_2O group. * $P < 0.05$ versus the air group (Dunnett's t -test; $N = 5$ for each group).

26.8 \pm 1.92 and 30.0 \pm 0.0 cmH₂O, respectively, for the control group. For the 70% N_2O group, the mean durations required to reach 15 cmH₂O were 12 and 27 min for MRN and SPN, respectively. Overall, significant relationships between sequential changes in cuff pressure and initial pressure were observed in all groups except the air group (control) for SPN.

Cuff pressures in the SPN groups were consistently higher than those in the MRN groups throughout this study. However, SPN could not maintain the intra-cuff pressure sufficiently when inflated with N_2O .

Approximations of deflation in cuff pressure were determined for the five gas groups (i.e., air, oxygen, 70%

N_2O , 50% N_2O , and 30% N_2O ; Tables 4 and 5). These approximations were assumed precise, as the coefficients of determination (R^2 values) were 0.9749–0.9990, except for SPN in the air group.

Tables 6 and 7 showed mean changes in cuff pressure over time for the TGM group. The composition of gases in this group was as follows: 25.7% N_2O /29.7% oxygen/44.6% nitrogen (ratio of 60% N_2O in oxygen to air = 4:3) [6]. For both MRN and SPN, the cuff pressures in the gas mixture group decreased significantly after 10 min compared with those in the air group; at 60 min, the cuff pressures reached 14.8 \pm 2.77 and 17.4 \pm 3.84 cmH₂O for MRN and SPN, respectively (Figures 3 and 4).

Discussion

In this study, we examined changes in cuff pressure following inflation of two types of tracheal tubes (MRN

Table 4. Approximation of MRN for the five gas groups. R^2 is the coefficient of determination; $E = 1 \times 10^{-9}$; X is the arbitrary time point (min); Y is the intracuff pressure at X .

Groups	Approximation	R^2
air	$y = -6E-06X^3 + 0.0008X^2 - 0.084X + 30$	0.9795
oxygen	$y = 7E-05X^3 - 0.0065X^2 + 0.0232X + 30$	0.9939
30% N ₂ O	$y = -0.0002X^3 + 0.0323X^2 - 1.572X + 30$	0.9990
50% N ₂ O	$y = -0.0001X^3 + 0.0218X^2 - 1.2258X + 30$	0.9984
70% N ₂ O	$y = -1E-05X^3 + 0.005X^2 - 0.6331X + 30$	0.9992

Table 5. Approximation of SPN for the five gas groups. R^2 is the coefficient of determination; $E = 1 \times 10^{-9}$; X is the arbitrary time point (min); Y is the intracuff pressure at X .

Groups	Approximation	R^2
air	$y = 30$	—
oxygen	$y = 2E-05X^3 - 0.0025X^2 + 0.0131X + 30$	0.9748
30%N ₂ O	$y = 5E-05X^3 - 0.0003X^2 - 0.5766X + 30$	0.9988
50%N ₂ O	$y = -6E-05X^3 + 0.0085X^2 - 0.6444X + 30$	0.9988
70%N ₂ O	$y = -2E-05X^3 + 0.0039X^2 - 0.3755X + 30$	0.9989

Table 6. Changes in the MRN cuff pressure for the TGM and air groups every 5 min for 60 min. The air group is the control group. Data is expressed mean \pm SD. * $P < 0.05$ versus the air group (Student's t -test; $N = 5$ for each group).

	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min
air	30	30	30	30	30	30	30	30	30	30	30	30
TGM	28.6 \pm 1.14	26.8 \pm 1.64*	25.8 \pm 2.28*	24.6 \pm 2.30*	23.6 \pm 2.30*	23.0 \pm 2.44*	21.8 \pm 2.86*	20.8 \pm 3.34*	20.0 \pm 4.06*	19.0 \pm 4.12*	18.0 \pm 4.12*	17.4 \pm 3.84*

Table 7. Changes in the SPN cuff pressure for the TGM and air groups every 5 min for 60 min. The air group is the control group. Data is expressed mean \pm SDs. * $P < 0.05$ versus the air group (Student's t -test; $N = 5$ for each group).

	5 min	10 min	15 min	20 min	25 min	30 min	35 min	40 min	45 min	50 min	55 min	60 min
air	29.6 \pm 0.89	29.4 \pm 0.89	28.6 \pm 1.14	28.6 \pm 1.14	28.4 \pm 1.51	28.0 \pm 1.58	28.0 \pm 1.58	27.8 \pm 1.64	27.2 \pm 1.78	27.0 \pm 2.12	26.8 \pm 1.92	26.8 \pm 1.92
TGM	28.6 \pm 1.14	26.8 \pm 2.16*	25.0 \pm 2.54*	23.4 \pm 2.07*	22.4 \pm 2.70*	20.8 \pm 2.58*	19.6 \pm 2.70*	18.6 \pm 3.50*	17.4 \pm 3.57*	16.6 \pm 2.88*	16.0 \pm 3.00*	14.8 \pm 2.77*

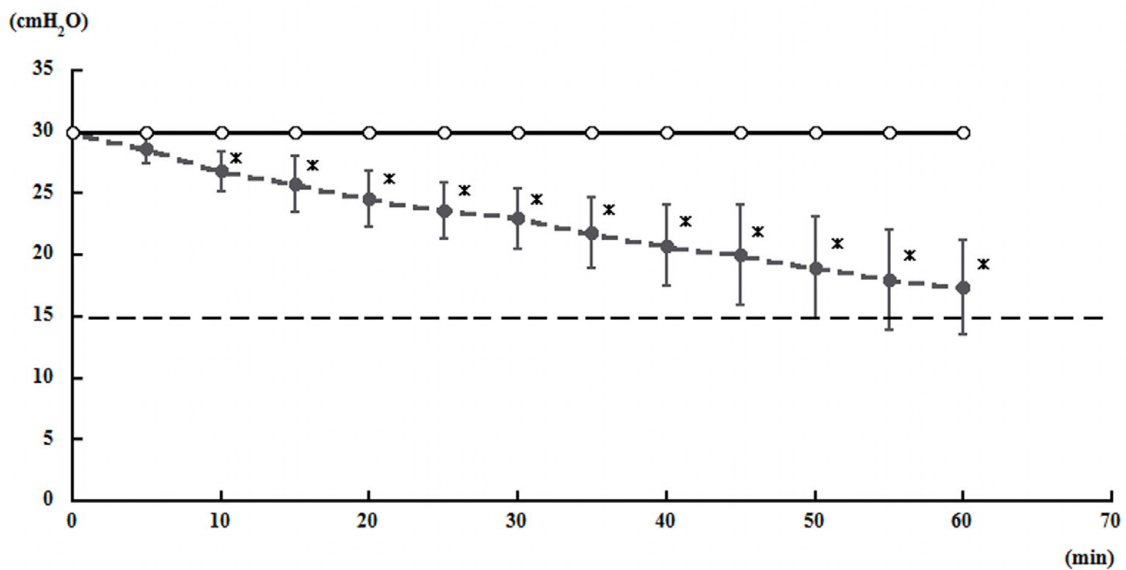


Figure 4. Changes in the SPN cuff pressure when the cuff was inflated with TGM. Data is expressed as mean \pm SD. Open circles represent the air group (control). Solid circles represent the TGM group. * $P < 0.05$ versus the air group (Student's t -test; $N = 5$ for each group).

and SPN) with different gases. Our data demonstrated that inflation with N₂O significantly decreased cuff pressures for both MRN and SPN; these data may help to predict cuff deflation in the clinical setting and provide insights into optimal use of N₂O during anesthesia.

During general anesthesia, the pressure of the endotracheal tube cuff may need to be changed; in particular, the use of N₂O during anesthesia results in increased cuff pressure due to the diffusion of N₂O into the cuff [7], leading to damage to the tracheal epithelium and tracheal wall. However, N₂O has major advantages for use during general anesthesia, facilitating rapid onset of anesthesia and improving recovery after anesthesia due to its low solubility in blood and adipose tissue. Furthermore, N₂O decreases the MAC of other volatile inhalational agents when used in combination with N₂O owing to the strong analgesic effects of N₂O. Thus, these properties of N₂O have led to the continued use of N₂O in modern clinical practice.

Various methods have been developed to limit the N₂O-dependent increase in cuff pressure. For example, several reports have described the use of a gas mixture containing

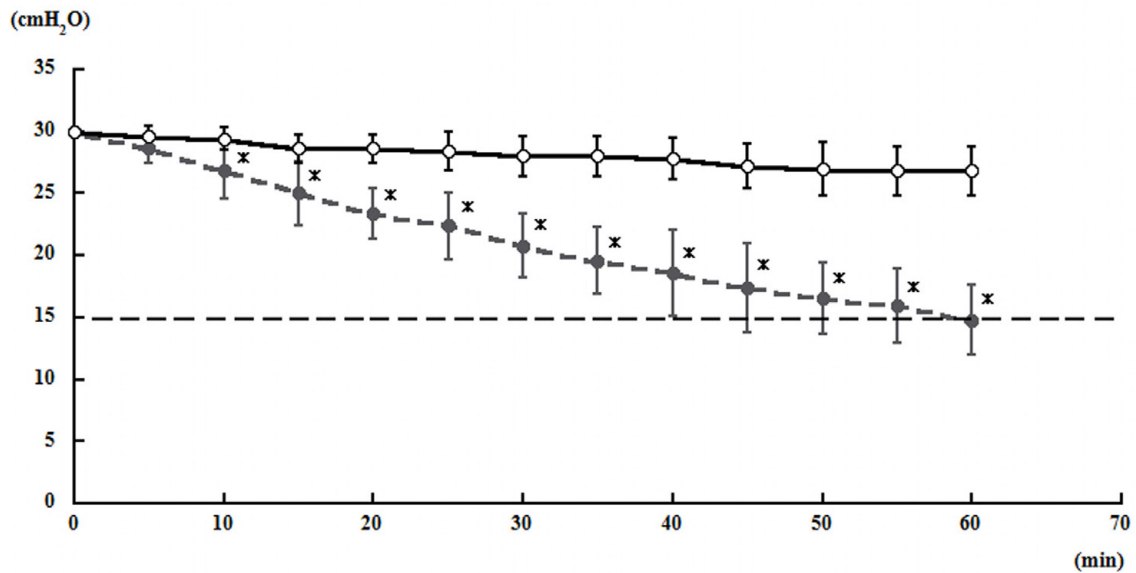


Figure 3. Changes in the MRN cuff pressure when the cuff was inflated with TGM. Data is expressed as mean \pm SD. Open circles represent the air group (control). Solid circles represent the TGM group. * $P < 0.05$ versus the air group (Student's *t*-test; $N = 5$ for each group).

the anesthetic gas with air or saline for inflation of the cuff [6,7]. Furthermore, specially designed tubes, such as the Brandt tracheal tube, which has a large pilot balloon that allows rediffusion of N_2O [8,9], or the Hi-Lo Tracheal Tube with the Lanz System, which automatically maintains a low intracuff pressure, have been developed. Other devices that also control cuff pressure have been described [10]. However, these methods are not commonly used because of their increased cost and personal preference [11].

Modern tracheal tube cuffs are usually made of polyvinyl chloride (PVC), which is permeable to N_2O . The MRN and SPN tubes used in this study were also made of PVC. Diffusion of N_2O into a cuff is dependent on the permeability coefficient of the cuff wall and is inversely proportional to the thickness of the cuff wall [12]. The mean cuff thickness of both MRN and SPN was 0.06 mm. In SPN, however, a plasticizer is added to soften the PVC and to make the cuff less permeable to N_2O [11]. In a previous study, SPN was shown to prevent the increase in intracuff pressure for 60 min after inflation of the cuff during N_2O anesthesia, suggesting that SPN should be used to prevent high tracheal wall pressure [11,13]. On the other hand, a study by Karasawa et al. suggested that the main mechanism through which SPN prevents the increase in cuff pressure may be the high compliance of the thinner cuff, rather than the N_2O gas-barrier properties [14]. In the current study, we found that cuff pressures were consistently higher when SPN was used than when MRN was used for all groups. Furthermore, higher concentrations of N_2O led to more rapid changes in cuff pressure. Remarkably, no change in cuff pressure was observed at 60 min when SPN was used. However, both MRN and SPN exhibited significant decreases in cuff pressure after about 5 min when N_2O was used to inflate the cuffs compared to that observed when air was used instead, suggesting that N_2O diffused out of the cuff

quickly.

In a previous study, Manabe et al. showed that use of the Portex Profile Cuffed tube from Smiths Medical during general anesthesia led to a decrease in cuff pressure to 12 cmH₂O at 60 min after inflation with inhalation gas (60% N_2O /40% oxygen) [6], similar to the results of the 50% N_2O in our study. Moreover, Manabe et al. reported that the cuff pressure of the mixture gas (inhalation anesthetic gas to air ratio = 4:3) exhibited almost no change during general anesthesia, measuring around 20 cmH₂O at 60 min [6]. The composition of the mixture gas used by Manabe et al. was 25.7% N_2O /29.7% oxygen/44.6% nitrogen, which is the same as that of the gas mixture used in our study. However, our results demonstrated a significant deflation of the cuff pressure when using MRN or SPN in the gas mixture group. Thus, from these results, we can conclude that MRN and SPN both allowed significant permeation of N_2O in and out of the cuff.

VAP is an infection related to mechanical ventilation [15] and has been reported to be the most prevalent nosocomial infection developing within 48 h of intubation in intensive care units [16]. The incidence of VAP is between 6% and 52% in intensive care units [17]. Among the factors predisposing patient to VAP, patient-related variables, including age and clinical condition, as well as treatment and care practices, such as enteral feeding and antacid prophylaxis, and factors related to infection control have been reported [18,19]. Moreover, decreased tube cuff pressure and cuff-stricture are associated with the etiology of VAP [5]. Thus, management of cuff pressure during general anesthesia and ICU management is important for prevention of VAP.

Our study used tracheal tube cuffs exposed to the atmosphere; this study model may be beneficial for the study of decreased cuff pressure. However, this study

is only a pilot study on VAP prevention, and further studies are required to determine whether these results translate to intubated patients during general anaesthesia or management in the intensive care unit. Currently in our laboratory, we are involved in a study of decreased cuff pressure during artificial ventilation.

In conclusion, SPN showed low permeability to N₂O. However, the cuff pressure decreased according to the concentration of N₂O. Consequently, we propose that anaesthesiologists must always consider cuff pressure when using N₂O. Indeed, a rapid decrease in cuff pressure may occur after administration of N₂O, which could increase the risk of VAP. Accordingly, it is essential to continually monitor cuff pressure during recovery from anaesthesia and while moving the patient after surgery.

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Conflicts of Interest

None.

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