An *in vitro* Method to Measure Permeability of Gases Through a Cuff Membrane of Tracheal Tube in Conditions Relevant to Its Clinical Uses

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The cuff pressure on a tracheal tube while being used in a clinical setting is affected by various physiological conditions. Hence, it is difficult to accurately assess the tracheal tube cuff membrane permeability for gases. We developed an experimental system that enabled accurate assessment of the transition and permeability of gases through a cuff membrane. To simulate nitrous oxide anesthesia, the partial pressure about a cuff membrane was considered separately in oral side, pulmonary side, and intracuff. The cuff pressure of a newly developed tracheal tube with gas barrier materials was assessed, and the permeability through the cuff membrane was evaluated. As a result, the study condition of Experiment II (the cuff was inflated with a gas mixture of 50% nitrous oxide and 50% oxygen) was the most appropriate in which the intracuff was inflated with the same gas mixure because of no concentration gradient between intra- and extra-cuff space. In the schematic diagram of the intracuff pressure changes during anesthesia with nitrous oxide, because of concentration gradient of the gas mixture, gases flow from pulmonary side into the cuff and in the latter phase gases pass through the cuff membrane. Our *in vitro* experimental system was revealed to be useful in accurately assessing the gas permeability through the cuff membrane of a tracheal tube in conditions relevant to clinical uses.

Key words: Permeability of the cuff membrane, Nitrous oxide, Gas barrier cuff

INTRODUCTION

High cuff pressure of the tracheal tube during anesthesia with nitrous oxide frequently leads to ischemic changes of tracheal mucosa, resulting in an edematous change of the vocal cord as well as the tracheal mucosa. Under tracheal mucosal morphological study, in healthy mongrel dogs investigation, Klainer *et al.* demonstrated that lateral wall pressure as low as 18 to 25 mmHg could produce these lesions in normotensive animals especially in as short as 2 hours [1-5]. Intracuff pressure increases during nitrous oxide gas anesthesia because the gas readily diffuses into the inside of cuff due to the high partial pressure gradient through the cuff membrane [6-8]. Recently tracheal tubes with a cuff using a membrane with a barrier function against the gas diffusion have been developed, and are commercially available. These tracheal tube have been evaluated for the nitrous oxide permeability and pressure changes of the cuff in a clinical setting [9-11]. However, the cuff pressure on a tracheal tube while being used in a clinical setting may be affected by various factors, including changes in temperature, blood pressure, sympathetic nervous system tonus and so on. These may complicate accurate assessment of tracheal tube cuff membrane permeability, thus making this measurement difficult to introduce into a clinical study. Furthermore, accurate assessment of the physical characteristics of the cuff membrane is difficult when merely measuring the change in the cuff pressure of an intubated tracheal tube in a clinical setting. We developed an experimental system that enabled accurate assessment of the transition and permeability of gases through a cuff membrane. Using this *in vitro* system, we studied the changes in tracheal tube cuff pressure under conditions relevant to clinical uses and evaluated a newly developed tracheal tube with a cuff membrane with a barrier function.

MATERIALS AND METHODS

1) Experimental Apparatus:

We used a closed 10-L plastic bucket as a chamber and connected it to the gas outlet of an anesthetic apparatus (Elite 60, Aika Co. Ltd., Japan), from which a mixed gas of nitrous oxide and oxygen was supplied at a rate of 6 L/min. The cuff portion of the tracheal tube was placed inside the chamber. The pilot balloon was connected to a cuff pressure-measuring system. The cuff inflating port was placed outside the chamber. The change in cuff pressure was measured with a transducer and the results were recorded on a chart via strain gauge amplifier. The temperature inside the chamber was monitored with a thermometer and maintained at 25 ± 1 °C. Gases from inside the chamber were vented through the tracheal tube and released from the end opposite of the tube (Fig. 1).

2) The tracheal tube:

An experimental tracheal tube was newly developed for this study by Fuji Systems Co. Ltd., Japan. As a gas barrier material in the cuff membrane, butyl rubber was used. This barrier material with 0.1 mm thickness

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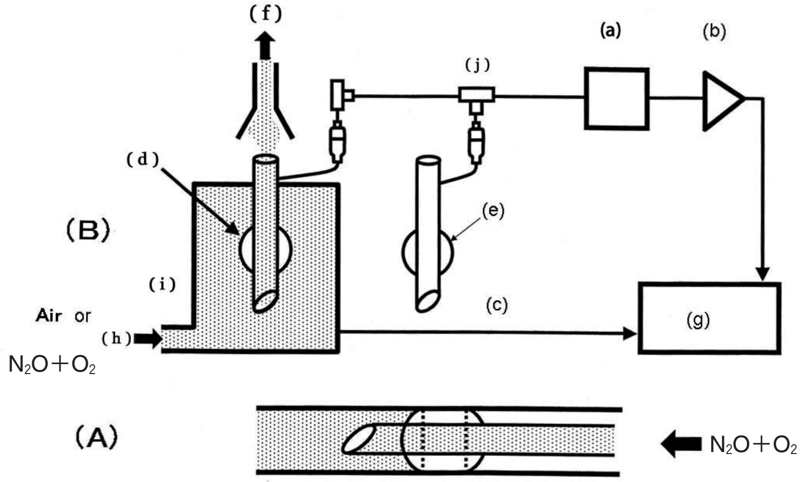

Fig. 1 (A) shows a tracheal tube cuff state in usual clinical nitrous oxide anesthesia. The (B) diagram of the nitrous oxide anesthesia *in vitro* experimental system designed to simulate clinical anesthesia with nitrous oxide. The cuff pressure was measured continuously with a transducer (a) and recorded on a chart (g) via a strain gauge amplifier (b). The temperature inside the chamber was monitored with thermometer (c) and maintained at 25 ± 1 °C. A chamber consisted of a closed 10-L plastic bucket (i). As a gas delivery system, air or mixed gas (50% nitrous oxide and 50% oxygen) supply at a rate of 6 L/min via the gas outlet of an anesthetic apparatus (Elite 60, Aika Co. Ltd., Japan) (h). To switch supply to the cuff with air or mixed gases three way stopcock (j) was placed.
In the (B) diagram, a tracheal tube cuff inside (d) and outside (e) of the chamber, reflected the pulmonary side and oral side, respectively of the tracheal tube. Gases from inside the chamber were vented through the endotracheal tube and released from the end opposite of the tube.

was sandwiched with silicone rubber membranes to form the cuff membrane with hardness of 20 shore as determined by a method by "Japanese Industrial Standards" (Fuji Systems Co. Ltd., Japan). The silicone rubber used in the new tube contains less silicone powder than that in the conventional tube.

3) Experimental designs:

Inside of the plastic bucket was filled with a mixed gas composed of 50% nitrous oxide and 50% oxygen supplied from an anesthetic apparatus.

Changes in the cuff pressure over time were measured with the initial cuff pressure at 40 cmH_2O. Changes in the cuff pressure were studied under following conditions.

Experiment I: The cuff was inflated with air

Experiment II: The cuff was inflated with a gas mixture of 50% nitrous oxide and 50% oxygen

Experiment III: Two tracheal tubes were connected to each other with one cuff placed inside the chamber and the other outside it, and the cuffs were inflated with air

Experiment IV: Two tracheal tubes were connected to each other with one cuff placed inside the chamber and the other outside it, and the cuffs were inflated with a gas mixture of 50% nitrous oxide and 50% oxygen

Gases diffuse and enter the cuff because of partial pressure gradients between the inside and the outside of the cuff [2, 3, 5].

4) Evaluation of a newly developed tracheal tube:

In order to evaluate our experimental tracheal tube with a gas barrier cuff, we conducted experiment II and compared the result with that in a conventional tracheal tube cuff consisted of silicone membranes (PHYCON®, Fuji Systems Co. Ltd., Japan). The mixed gas inside and outside the cuff was composed of 50% nitrous oxide and 50% oxygen, and changes in the cuff pressure over time were measured with the initial pressure set at 40 cmH_2O.

RESULTS

1) Comparison between experiments I and III

The results from experiments I and III were compared. In both experiments the same gas barrier cuff was used with the cuff inflated with air. The only difference was whether the cuff was placed either inside (experiment I) or both inside and outside (experiment III) the chamber. In both experiments, the cuff pressure initially increased followed by a subsequent decrease after reaching a peak. However, the decrease was more rapid in experiment III.

2) Comparison between experiments II and IV

The results from experiments II and IV were compared. In both experiments, the same gas barrier cuff was used and the cuff was inflated with a gas mixture of 50% nitrous oxide and 50% oxygen. The only difference was whether the cuff was placed either inside (experiment II) or both inside and outside (experiment IV) the chamber. The cuff pressure gradually decreased without any initial increase in both experiments. However, the decrease was more rapid in experiment IV.

3) Comparison between experiments I and II

The results from experiments I and II were com-

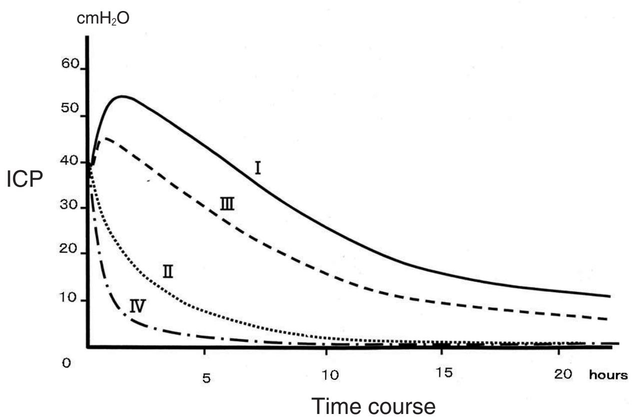

Fig. 2 Changes in the intra-cuff pressure when inflated with air or with a gas mixture of 50% nitrous oxide and 50% oxygen. The effect of connecting another tracheal tube outside the chamber was seen in Exp. III and IV. The only difference in Exp. I and III was whether the cuff was placed either inside (Exp. I) or both inside and outside (Exp. III) the chamber. ICP; intra-cuff pressure (cmH_2O).

pared. This is a comparison between an air-inflated cuff (experiment I) and a cuff inflated with a gas mixture of 50% nitrous oxide and 50% oxygen (experiment II). The cuff pressure initially increased in experiment I followed by a subsequent decrease, which was slower than that observed in experiment II (Fig. 2).

In a clinical situation, the cuff is initially inflated with air after intubation. With the environment of the experiment set at 1 atmospheric pressure and 37 °C, the cuff pressure was initially at 790 mmHg (760 + 30 mmHg). Likewise, in experiment I, the cuff contains the air, which is composed of PN_2 at 620 mmHg and PO_2 at 170 mmHg, at 1 atmospheric pressure and 37 °C (Fig. 3A).

Outside the cuff or inside the plastic chamber, is composed of a gas mixture of 50% nitrous oxide and 50% oxygen which means PN_2O 380 mmHg and PO_2 380 mmHg. Because of the partial pressure gradient of gases across the cuff membrane, nitrogen should exit and nitrous oxide and oxygen should enter the cuff by diffusion through the cuff membrane. In contrast, when the cuff was initially inflated with a gas mixture of 50% nitrous oxide and 50% oxygen (PN_2O 395 mmHg and PO_2 395 mmHg), in experiments II, the cuff pressure decreased more rapidly. The gases would exit the cuff because of the partial pressure gradient of the gases across the cuff membrane. In addition, nitrous oxide and oxygen would be released into the atmosphere (Fig. 3B).

In experiment III the second cuff was placed in the air, which is composed mainly of nitrogen at 620 mmHg and oxygen at 170 mmHg. Under these conditions, gases within the cuff would exit, resulting in a rapid decrease in the cuff pressure (Fig. 4). In contrast, the cuff pressure decreased more rapidly when the cuff was initially inflated with a gas mixture of 50% nitrous oxide and 50% oxygen.

4) Comparison between a new experimental tracheal tube and a conventional tube

Using our system, we evaluated the newly developed tracheal tube with a cuff membrane with a barrier function. The change in cuff pressure of our experimental tracheal tube was compared with that in a conventional tube (PHYCON® Fuji Systems Co. Ltd., Japan) with the cuffs placed in and filled with a gas mixture of 50% nitrous oxide and 50% oxygen. The cuff pressure of the newly developed experimental tracheal tube was more stable than that of the conventional one (Fig. 5). The time for the cuff pressure to decrease to the half level of the initial pressure was one hour with PHYCON® tube, and it prolonged a half hour longer with the newly developed tube.

DISCUSSION

The tracheal tube cuff pressure while being used in a clinical setting is affected by various physiological factors [12–13]. Therefore, accurate assessment of the physical characteristics of the cuff membrane is difficult when merely measuring the change in the cuff pressure of an intubated tracheal tube in a clinical setting. We developed an *in vitro* experimental system to accurately assess the barrier characteristics of the tracheal tube cuff against a mixed gas of nitrous oxide and oxygen. Using an experimental system, the transition of gases within the tube cuff was investigated under various conditions.

A diagram of the connected tracheal tubes used in experiments III and IV is presented in Fig. 1. The tube cuffs placed inside and outside the chamber reflect the pulmonary side (P_L) and oral side (P_O), respectively, of a cuff in a clinical situation during general anesthesia with nitrous oxide. This allows the system to be an appropriate *in vitro* model for laboratory investigations of general anesthesia with nitrous oxide. The cuff were inflated with air in experiment III, which is clinically relevant.

Because of partial pressure gradient of the gas through the cuff membrane, nitrogen and oxygen would enter the cuff although its permeability is low [14]. The membrane permeability of nitrous oxide is higher as compared to the other gases. In addition, the partial pressure gradient across the cuff membrane is initially large, causing a rapid inflow of nitrous oxide and a subsequent increase in the cuff pressure (Fig. 6, phaseA). The initial rise in the cuff pressure itself would produce a corresponding increase in tension on the membrane wall. The increased tension would eliminate its contents, promoting deflation of the cuff. In other words, nitrous oxide diffuses in the cuff membrane and is subsequently eliminated together with air by diffusion in the opposite direction. Air is replaced with a mixed gas mainly composed of nitrous oxide (Fig. 6, phaseB). As long as membrane tension exists, the partial pressure through the cuff would be higher than that outside the cuff. The elimination of nitrous oxide would exceed its inflow and then the cuff would start to deflate. The observed peak in the cuff pressure would be a result of this phenomenon.

The difference between experiments I and II was that the cuff was inflated with air in experiment I, where the cuff was inflated with 50% nitrous oxide

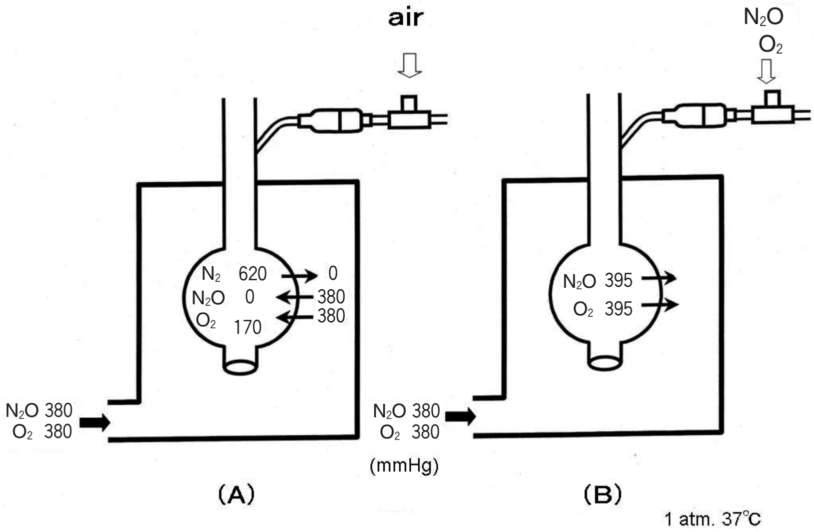

Fig. 3 Illustration in Exp. I and II (A): Transition of gases through the cuff membrane in experiment I (air in the cuff) at 1 atmospheric pressure and 37 °C, with the initial cuff pressure at 40 cmH_2O. (**B**): Transition of gases through the cuff membrane in experiment II (nitrous oxide and oxygen in the cuff) at the same condition.

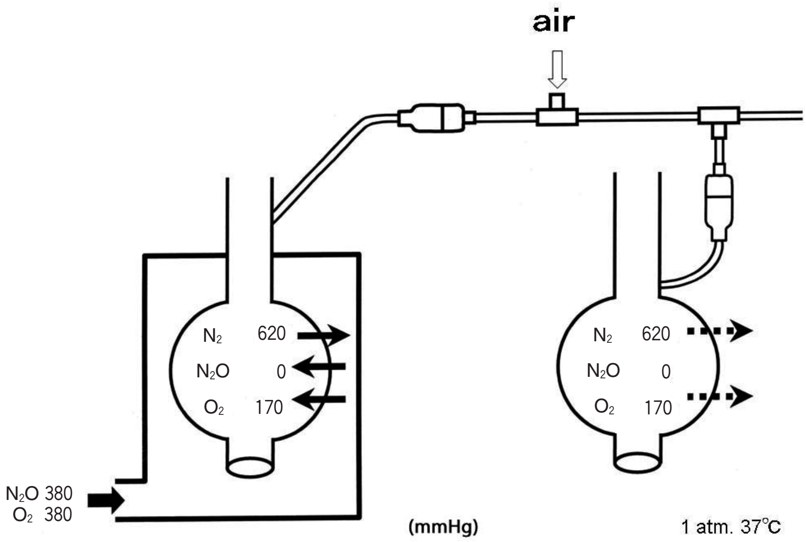

Fig. 4 Illustration in Exp. III
The tracheal tube cuff was placed both inside and outside the chamber. Transition of gases through the cuff membrane in experiment III (cuff was inflated with air).

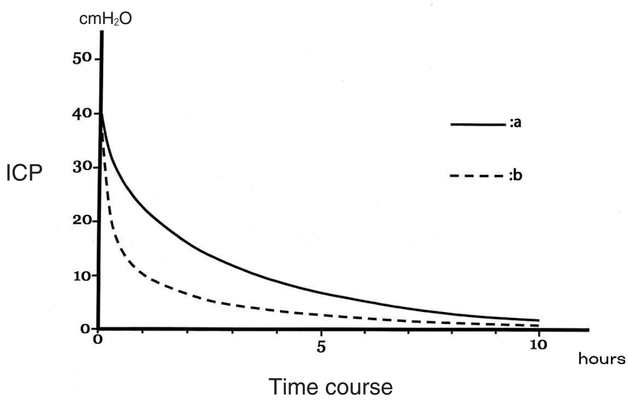

Fig. 5 Comparison of gas permeability between the newly developed tracheal tube with a gas barrier materials (a) and a conventional tracheal tube (PHYCON ® Fuji Systems Co. Ltd., Japan) (b). The cuff pressure of the newly developed tracheal tube with a gas barrier materials was assessed by the *in vitro* method where the cuff was inflated with a gas mixture of 50% nitrous oxide and 50% oxygen in the condition. ICP: intra-cuff pressure (cmH_2O).

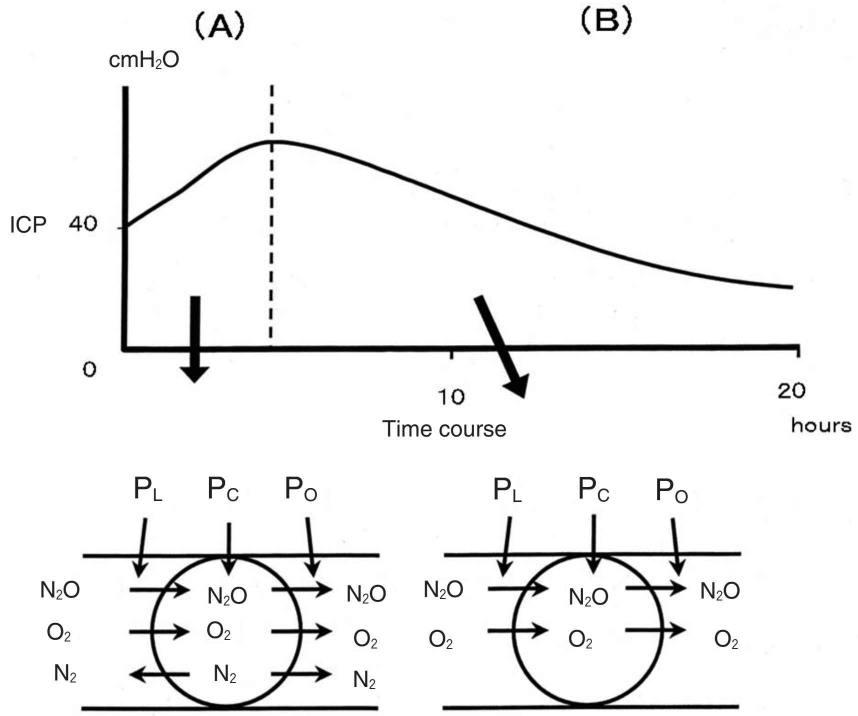

Fig. 6 The intracuff pressure changes in a clinical situation during anesthesia with nitrous oxide.
Phase (**A**); The early phase after cuff inflation with air was produced by inflow of nitrous oxide due to partial pressure gradient and/or increased cuff pressure. Phase (**B**); The latter phase after cuff inflation with air was produced by elimination of gases from inside the cuff and/or decreased cuff pressure.
"P_L", "P_O" and "P_C" represent the pulmonary side, oral side and intracuff, of the tube cuff, respectively, in an anesthesia with nitrous oxide model (cuff was inflated with air).

and 50% oxygen in experiment II. In experiment I, the cuff pressure initially increased followed by a subsequent decrease after reaching a peak. The cuff pressure peak may be caused by the initial entry of nitrous oxide, due to the partial pressure gradient, which was followed by decrease, caused by subsequent exiting of nitrous oxide, due to the increase in the cuff tension by the initial entry of nitrous oxide. This decrease was slower than that observed in experiment II. This is probably caused by slower exiting of oxygen and nitrogen due to a low permeability of these gases than that of nitrous oxide. This suggests that nitrous oxide would become the dominant component quite some time after the cuff pressure reaches its peak.

This study demonstrated the advantage of inflating the cuff with nitrous oxide and oxygen over that with air against the cuff pressure increase. This is in agreement with previous reports on clinical settings. Raeder *et al.* [6], Stanley *et al.* [17] and Revenäs *et al.* [7] reported that the cuff pressure increased during nitrous oxide/oxygen anesthesia when the tracheal tube cuff was inflated with air, whereas the increase was prevented when nitrous oxide/oxygen was used to inflate the cuff. Karasawa *et al.* [11] reported a new tracheal tube with N_2O gas barrier properties, inhibits an increase in the cuff pressure during N_2O anesthesia because of the high compliance of the cuff, rather than the gas barrier properties. Mitchell *et al.* [15] reported that cuff pressure increased during nitrous oxide/oxygen anesthesia when air was used to inflate the cuff, and decreased slightly when nitrous oxide/oxygen was used, suggesting a minor gas leak, and was virtually maintained at its initial level when physiological saline was used. The results of these studies indicate that cuff inflating with the same gas mixture used for anesthesia or with physiological saline may be an effective measure against cuff pressure increase. Cross *et al.* [16] developed. an equation of Pic = Ptw + Pf (d, s) about the assay of the cuff pressure for the nitrous oxide anesthesia case in the clinical example and the trachea sidewall pressure. Pic: cuff pressure, Ptw: tracheal wall pressure, d: pressure by the diameter of the cuff, s: the hardness of cuff materials.

With the optimal conditions to accurately assess the gas permeability through a cuff membrane, a newly developed tracheal tube cuff was evaluated. The *in vitro* system demonstrated that the cuff pressure of it was more stable than a conventional one. The silicone rubber itself contained less silica powder than that used in conventional cuff membranes. This may also be advantageous in improving the gas barrier characteristics of the cuff membrane because it renders the silicone rubber softer and less permeable to gases. This experiment is a basic study to clarify a diffusive trend of the gas through the tracheal tube cuff membrane during general anaesthesia with nitrous oxide. There were many reports in which the trachea wall pressure and intracuff pressure were measured in the artificial trachea model. Chandler M. *et al.* described a concept of three gas components across the cuff membrane and explained partial pressure gradient across the membrane.

We, therefore, composed an experimental system to analyze three gas compositions as an independent space using two tracheal tubes in this study. This is the first report in that the gas movement across the tracheal tube cuff membrane can be detected with the experimental device. We can measure and explain how partial pressure differences occur between pulmonary side, oral side, and in the tracheal tube across the cuff membrane in our *in vitro* experimental model. And as a result, we can also explain how cuff pressure changes.

In conclusion, our *in vitro* experimental system was useful in assessing the gas permeability through the cuff membrane of a tracheal tube in conditions relevant to clinical uses. Using this system, new approaches to develop tracheal tube cuff with a function that would prevent increases in the cuff pressure should be investigated, and newly developed tubes should be evaluated before they are introduced into clinical uses.

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REFERENCES

1) Klainer AS, Turndorf H, Wu W, Maewal H, Allender P. Surface alteration due to endotracheal intubation Am J Med 1975; 58: 674-83.
2) Ferdinande P, Kim DO. Prevention of postintubation laryngotracheal stenosis. Acta Otorhinolaryngol Belg. 1995; 49: 341-6.
3) Lewis FR Jr, Schiobohm RM, Thomas AN. Prevention of complications from prolonged tracheal intubation. Am J Surg. 1978; 135: 452-7.
4) Stauffer JL, Olson DE, Petty TL. Complications and consequences of endotracheal intubation and tracheotomy. A prospective study of 150 critically ill adult patients. Am J Med. 1981; 70: 65-76.
5) Seegobin RD, van Hasselt GL. Endotracheal cuff pressure and tracheal mucosal blood flow: endoscopic study of effectsof four large volume cuffs. Br Med J (Clin Res Ed). 1984; 288: 965-8.
6) Raeder JC, Borchgrevink PC, Sellevold OM. Tracheal tube cuff pressures (The effects of different gas mixtures.). Anesthesia 1985; 40: 444-447.
7) Revenäs B, Lindholm CE. Pressure and volume changes in tracheal tube cuffs during anaesthesia: Acta anaesthesiol Scand. 1976; 20: 321-326.
8) Tu NH., Saidi N, Leiutaud T, Bensaid S, Menival V, Duvaldestin P. Nitrous oxide increases endotracheal cuff pressure and the incidence of tracheal lesions in anesthetized patients Anesth Analg. 1999; 89: 187-190.
9) Kitamura A, Yamada K, Ishihara Y, Ogawa R. The Intracuff pressure changes in N2O gas – barrier cuff made of a special material Masui. 1993; 42: 826-30. (Japanese)
10) Sato K. Tanaka M. Nishikawa T. Changes in intracuff pressure of endotracheal tubes permeable or resistant to nitrous oxide and incidence of postoperative sore throat. Masui 2004; 53: 767-771.
11) Karasawa F. Mori T. Okuda T. Satoh T. Profile soft seal cuff, a new endotracheal tube, effectively inhibits an increase in the cuff pressure through high compliance rather than low diffudion of nitrous oxide. Anesth Analg 2001; 92: 140-4.
12) Plunkett PF. Perrault SA. The effect of tracheal shape on the pressure dynamics of seven commercially available Endotracheal tube cuffs: An *in vitro* study. Respir Care 1981; 26: 45-52.
13) Janet T. Mary H. Donna J. Barbara M. Artificial airways: a survey of cuff management practice. Heart & lung 1996; 25: 225-235.
14) Chandler M. Pressure changes in tracheal tube cuffs. Anaesthesia 1986; 41: 287-293.
15) Mitchell V, Adams T, Calder I. Choice of cuff inflation medium during nitrous oxide anaesthesia. Anesthesia 1999; 54: 32-36.
16) Cross ED. Recent development in tracheal cuffs. Resuscitation 1973; 2: 77.
17) Stanley TH. Liu WS. Tracheostomy and endotracheal tube cuff volume and pressure changes during thoracic operations. Ann Thorac Surg 1975; 20: 144.