Anesthesiology 2001; 95:1120–4

Intracuff Pressure and Tracheal Morbidity

Influence of Filling Cuff with Saline during Nitrous Oxide Anesthesia

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Background: **Diffusion of nitrous oxide into the cuff of the endotracheal tube results in an increase in cuff pressure. Excessive endotracheal tube cuff pressure may impair tracheal mucosal perfusion and cause tracheal damage and sore throat. Filling the cuff of the endotracheal tube with saline instead of air prevents the increase in cuff pressure due to nitrous oxide diffusion. This method was used to test whether tracheal morbidity is related to excess in tracheal cuff pressure during balanced anesthesia.**

Methods: **Fifty patients with American Society of Anesthesiologists physical status I or II were randomly allocated to two groups with endotracheal tube cuffs initially inflated to 20–30 cm H_2O with either air (group A) or saline (group S). Anesthesia was maintained with isoflurane and nitrous oxide. At the time of extubation, a fiberoptic examination of the trachea was performed by an independent observer, and abnormalities of tracheal mucosa at the level of the cuff contact area were scored. Patients assessed their symptoms (sore throat, dysphagia, and hoarseness) at the time of discharge from the postanesthesia care unit and 24 h after extubation on a 101-point numerical rating scale.**

Results: **Cuff pressure increased gradually during anesthesia in group A but remained stable in group S. The incidence of sore throat was greater in group A than in group S in the postanesthesia care unit (76 *vs.* 20%) and 24 h after extubation (42 *vs.* 12%; $P < 0.05$). Tracheal lesions at time of extubation were seen in all patients of group A and in eight patients (32%) of group S ($P < 0.05$).**

Conclusion: **Excess in endotracheal tube cuff pressure during balanced anesthesia due to nitrous oxide diffusion into this closed gas space causes sore throat that is related to tracheal mucosal erosion.**

LARYNGOTRACHEAL morbidity is frequent after tracheal intubation, even with short-duration anesthesia. The main symptom reported after tracheal intubation is sore throat, but patients also report hoarseness and dysphagia. Although the exact physiopathology of postintubation airway symptoms is not fully elucidated, mucosal damage occurring at the cuff level is thought to be an important causative factor for tracheal morbidity. Decrease in tracheal mucosa perfusion occurs when the cuff exerts pressure greater than 30 cm H_2O. This is probably the first step in development of mucosal damage.[1,2] The use of nitrous oxide (N_2O), which is well-known to diffuse into endotracheal tube cuffs, and the lack of frequent control of intracuff pressure during the perioperative period are the most important factors that contribute to the high incidence of excessive intracuff pressures during this period.[3,4] In a recent clinical study, filling the endotracheal tube cuff with an N_2O–air gas mixture prevented excessive cuff pressure and reduced tracheal injury.[5] However, significant variations of inspired N_2O concentration observed during balanced anesthesia maintenance resulted in either deflation or overinflation of the cuff.[5,6] An alternative method to prevent N_2O-induced variations in intracuff pressure has been described in an animal model.[7] Filling the tracheal probe cuff with saline was shown to reduce tracheal mucosal membrane damage. Recent clinical studies reported the use of this method to prevent high intracuff pressure and postoperative airway symptoms.[8–10] Although decreasing or maintaining intracuff pressure below tracheal mucosa capillary pressure is mandatory, clinical evidence of the efficacy of this practice in preventing tracheal morbidity is lacking. In this clinical human study, we hypothesized that maintaining low intracuff pressure using saline to fill the cuff would decrease the incidence of postoperative laryngotracheal discomfort and tracheal mucosal lesions in anesthetized patients.

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Materials and Methods

After we received approval from the local ethics committee (Comité Consultatif de Protection des Personnes dans la Recherche Biomédicale, Henri-Mondor, Créteil cedex, France) and written informed consent, 50 nonsmoking adult patients with American Society of Anesthesiologists physical status I or II were enrolled in a prospective, randomized, double-blind study. All patients were scheduled for surgical procedures during general anesthesia with an expected duration of 90 min or more. Patients undergoing head or neck surgery or requiring placement of a nasogastric tube were excluded from the study. Sterile endotracheal tubes (Lo-Contour;

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Received from the Department of Anesthesia, Hôpital Henri Mondor, Créteil, France. Submitted for publication December 18, 2000. Accepted for publication May 29, 2001. Support was provided solely from departmental sources. Presented in part at the annual meeting of the American Society of Anesthesiologists, Dallas, Texas, October 9–13, 1999.

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Mallinckrodt, Athlone, Ireland) with high residual volume, low-pressure cuff, and an ID of 7.5 mm for female and 8.0 mm for male patients were used. All patients were premedicated with 50–100 mg hydroxyzine administered orally approximately 1 h before induction. Standard clinical monitoring was performed. After preoxygenation for 4 min, anesthesia was induced with fentanyl (3 μg/kg body weight) and propofol (2 mg/kg body weight), both administered intravenously. Patients were paralyzed with a nondepolarizing relaxant, and tracheal intubation was performed by an experienced anesthesiologist after approximately 3 min of mask ventilation when maximum neuromuscular blocking effect assessed by the train-of-four count at the adductor pollicis was achieved. A Guedel airway was used for all patients during anesthesia. Patients were excluded if more than one trial was needed for intubation. Patients were randomly assigned, by opening a sealed envelope, to one of two groups. In group A, the endotracheal cuff was inflated with air, and in group S, the endotracheal cuff was inflated with saline. The cuff in group A was connected to a manometer (Mallinckrodt), and the cuff in group B was connected to a pressure transducer (Becton Dickinson Critical Care Systems, Singapore). In both groups, the cuff was initially inflated to achieve a cuff pressure of 20–30 cm H_2O without further manipulation during the anesthetic procedure. Mechanical ventilation was controlled and adapted to maintain end-tidal carbon dioxide at 4.5 ± 0.5%. Anesthesia was maintained with isoflurane (0.5–1.5% end-tidal) and 66% N_2O in oxygen. Additional boluses of fentanyl (1–2 μg/kg) were administered to maintain surgical analgesia. Nondepolarizing agent was reinjected when continuous muscle relaxation was necessary. Before tracheal extubation, patients breathed 100% oxygen for 5 min. At the time of extubation, fiberoptic examination (LF-T fiberscope; Olympus, Rungis, France) of the trachea *via* the endotracheal tube was performed by an observer unaware of the patient group. As the endoscope went below the extremity of the endotracheal tube, the cuff was deflated. If any reactivity to endotracheal tube cuff deflation was observed, propofol (50 mg) was injected intravenously before extubation was performed. The endotracheal tube and the endoscope were gently withdrawn, and the aspect of the trachea in relation to the cuff contact area was then assessed according to the following score: 0 = normal; 1 = one mucosal ulceration; 2 = several mucosal ulcerations (see Web Enhancement for video and pictures illustrating the different kinds of lesions). Intravenous proparacetamol and morphine were used for postoperative analgesia in the recovery room. At the time of discharge from the postanesthesia care unit and 24 h after the end of anesthesia, the patients were asked about laryngopharyngeal discomfort by an independent observer unaware of the patient groups and the results of tracheal fiberoptic examination. Three symptoms were distinguished: sore throat, dysphagia, and hoarseness. Patients assessed the severity of their symptoms on a 101-point numerical rating scale (0 = no discomfort; 100 = worst discomfort possible).

Statistical Analysis

We calculated that 25 patients were required in each group to detect a decrease in incidence of postoperative sore throat from 70% to 35% with a power of 0.8 and for a type I error α of 0.05. Continuous data were compared using the Mann–Whitney U test and the Wilcoxon rank sum W test for independent samples. Differences in incidence of laryngotracheal symptoms and severity of mucosal lesions between the two groups were compared using the chi-square test or the Fisher exact test for small samples as required. Two-way analysis of variance was used for comparison of repeated measures of cuff pressure. Results are reported as mean ± SD. $P < 0.05$ was considered statistically significant.

Results

Both groups were similar regarding patient details and anesthetic characteristics (table 1). The intraoperative course and recovery from anesthesia were uncomplicated in all patients. As shown in figure 1, the cuff pressure in group A increased steadily throughout the procedure, whereas it remained stable in group S (two-way analysis of variance, $P < 0.05$). At time of extubation, four patients in group S and six patients in group A received a bolus of propofol because of airway reactivity due to the cuff deflation. The incidence of sore throat was lower in group S than in group A in the postanesthesia care unit and at 24 h (fig. 2). The incidence of dysphagia and hoarseness was similar for the two groups in the postanesthesia care unit and at 24 h (fig. 2). The intensity of sore throat, hoarseness, and dysphagia was not different between the two groups (table 2). The incidence and severity of tracheal mucosal lesions were

Table 1. Anthropometric and Perioperative Data

	Group A (n = 25)	Group S (n = 25)
Age (yr)	54 ± 20	58 ± 21
Sex (M/F)	13/12	11/14
Weight (kg)	68 ± 14	69 ± 13
Height (cm)	165 ± 7	167 ± 9
Duration of anesthesia (min)	150 ± 50	162 ± 45
Duration of intubation (min)	200 ± 60 [190]	232 ± 99 [225]
Peroperative fentanyl (μg)	421 ± 160	380 ± 187
Morphine in PACU (mg)	6 ± 6	6 ± 5
First day morphine administration in the ward (mg)	6 ± 7	6 ± 6

Data are mean ± SD [median]. There were no significant differences between both groups.

PACU = postanesthesia care unit.

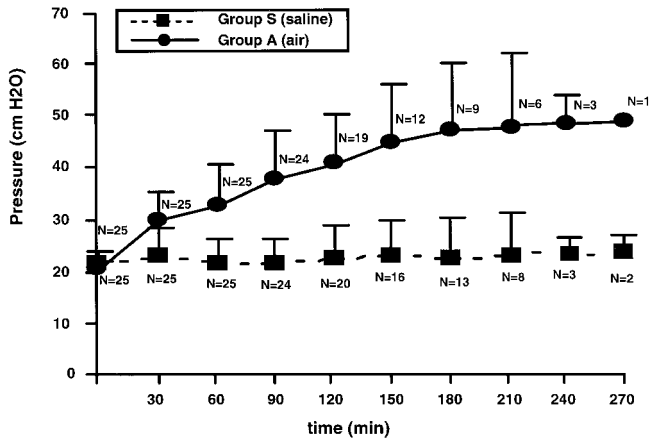

Fig. 1. Cuff pressures (mean ± SD) in each group during nitrous oxide anesthesia.

higher in group A than in group S (table 3), and a significant relation (chi-square, $P < 0.05$) between sore throat occurrence and severity of endoscopic tracheal lesions was found (table 4).

Discussion

Our data show that during N_2O anesthesia, filling the cuff with saline instead of air results in stable intracuff pressure, lower incidence of sore throat, and fewer endoscopic tracheal lesions. The current results reinforce the assumption that when inflation of the cuff is monitored, N_2O becomes the principal causative factor of overpressure in the endotracheal tube cuff during balanced anesthesia. Indeed, the high solubility of N_2O in blood induces a large gradient of diffusion between blood and an air-filled cuff. Conversely, *in vitro* animal studies showed that when saline was used to fill the cuff, the lack of pressure increase secondary to N_2O diffusion depended on the physical principle that liquids do not expand in volume when highly soluble gases dissolve in them.[7,11]

In our study, tube cuffs were arbitrarily inflated to a pressure not exceeding 30 cm H_2O because it has been shown in humans that tracheal mucosal blood flow is impaired when cuff pressure increased above this value.[12] Cuff pressure remained stable in the patients in the saline group, whereas all the patients in the air group had cuff pressures that exceeded 40 cm H_2O at some time during anesthesia, which was likely to cause compromised tracheal capillary mucosal perfusion. In an animal model, cuff pressure greater than 30 cm H_2O for 15 min was sufficient to induce histologic tracheal mucosal lesions, which did not worsen with time beyond 15 min.[1] These experimental observations can be paralleled with the results of our clinical study. Prevention of overpressure of the endotracheal tube cuff can be achieved by several means. First, frequent measurement and adjustment of cuff pressure has been recommended, but this method requires a specific manometer and is time consuming.[13] An endotracheal tube with a pressure-regulated cuff system like the Brandt Anesthesia Tube is an effective method to prevent increased intracuff pressure but has a prohibitive cost.[14] It has also been proposed to fill the cuff of the endotracheal tube with the inhaled anesthetic gas mixture. A recent study showed that postintubation tracheal mucosal lesions were less common when tube cuffs were filled with an N_2O–oxygen gas mixture.[5] However, large variations in inspired N_2O concentration associated with the different phases of anesthesia induced rapid changes in cuff volume, resulting in either overinflation or deflation.[5,6] Finally, as demonstrated in experimental setting, filling the cuff with saline seems to be a valuable method to provide constant cuff pressure during N_2O anesthesia independently of changes in inspired N_2O concentration.[6] We have used this technique for the purpose of our study; however, we do not recommend this technique in routine clinical practice because the endotracheal tube cuff was not designed to be filled with saline.

Using fiberoptic inspection of the trachea, we showed that there is a correlation between tracheal mucosal lesions and sore throat. To our knowledge, this is the first demonstration of a relation between cuff overpressure, tracheal mucosal "injury," and sore throat. Reasons

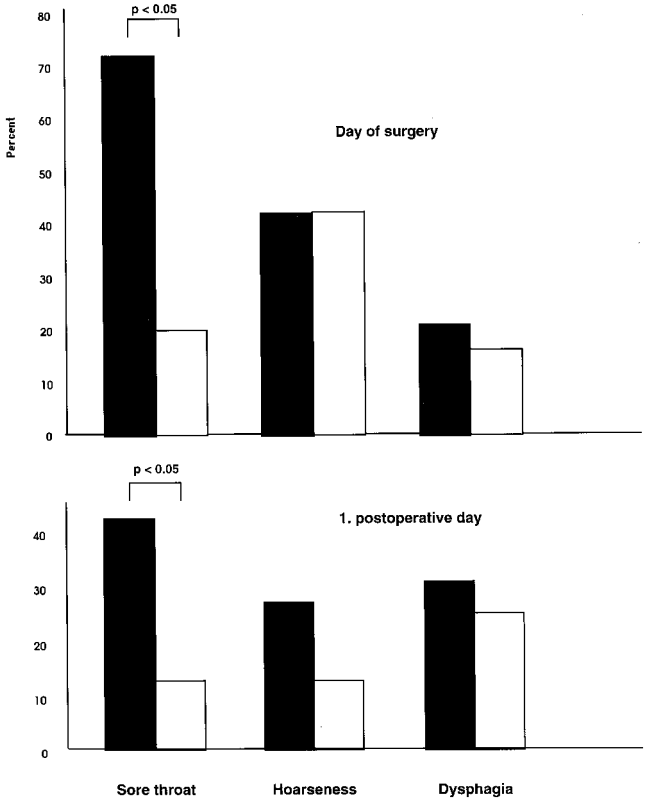

Fig. 2. Incidence of sore throat, hoarseness, and dysphagia in the saline group (open bars) and in the air group (filled bars).

Table 2. Patient Assessment of Symptoms on a 101-Point Numerical Rating Scale

	Sore Throat		Hoarseness		Dysphagia	
	Day of Surgery	Postoperative Day 1	Day of Surgery	Postoperative Day 1	Day of Surgery	Postoperative Day 1
Saline	28 ± 13 (n = 6)	20 ± 16 (n = 3)	40 ± 23 (n = 10)	36 ± 17 (n = 3)	26 ± 16 (n = 4)	30 ± 12 (n = 6)
Air	26 ± 12 (n = 18)	30 ± 10 (n = 11)	36 ± 20 (n = 10)	25 ± 12 (n = 6)	34 ± 9 (n = 5)	35 ± 11 (n = 7)

Data are mean ± SD (n is number of patients with complaints).

for these relations must be discussed. Regarding N_2O anesthesia and cuff overpressure, experiments both *in vitro* and *in vivo* have shown that cuff permeability to N_2O allowed the intracuff pressure to increase because of a net influx of N_2O in an air-filled cuff.[3,4] Moreover, the effect of endotracheal tube cuff pressure overlapping tracheal capillary mucosal perfusion was demonstrated in experimental settings.[1]

Focusing now on the cuff overpressure–sore throat relation, conflicting findings have been published. Some reports showed that sore throat was more frequent after the use of low-pressure, high-residual-volume cuffs than with high-pressure, low-residual-volume cuffs.[15–17] Differences in the cuff-contact tracheal area between different kinds of cuffs may provide explanations for these observations. A recent negative study failed to show any protective effect of limiting endotracheal tube cuff pressure on postintubation sore throat incidence.[8] However, the study design, which may have altered the authors' conclusions, differs greatly from our protocol in that anesthetic technique and intubating conditions were not controlled and most patients had a gastric tube inserted. The authors illustrated the problem of combining potential confounding factors in the anesthetic and upper airway management for relating sore throat to tracheal cuff pressure. Conversely, several clinical studies have shown that the incidence of postoperative sore throat was significantly decreased when low cuff pressure was maintained during anesthesia, suggesting that for a constant cuff-tracheal surface area, intracuff pressure was the determining factor for postintubation sore throat.[10,14] Our results support these findings.

In the current study, patients requiring gastric tube insertion were not included, and only easily intubated patients were studied. The anesthetic protocol was controlled. Neuromuscular blockade was monitored, and extubation was performed after relaxant reversal. With a methodologic rigor in the patient's selection and airway management, we have demonstrated that high tracheal cuff pressure was an important factor in the development of tracheal mucosal lesions whose severity was correlated to postoperative throat incidence. Other postoperative symptoms related to tracheal intubation and airway management are currently described, including principally hoarseness and dysphagia. The incidence of these symptoms was similar between the two groups, suggesting that they are not related to cuff pressure.

In the current study, sore throat, when present, was of the same intensity between the two groups. From the 101-point-scale evaluation, sore throat was considered to be moderate. Sore throat has even been considered to be a minor unavoidable complication of general anesthesia.[18] The low intensity of sore throat generated during tracheal intubation, particularly when overpressure occurs, is not a reason to neglect this phenomenon, especially in view of the tracheal lesions currently observed. Because it has already been recommended, control of the pressure of the endotracheal tube cuff throughout anesthesia should be performed and will limit the incidence of postoperative sore throat.[13]

In conclusion, excessive pressure in the cuff of the endotracheal tube, which is mainly generated by the diffusion of N_2O, is responsible for tracheal mucosal erosions and postoperative sore throat. Although sore throat after short-term intubation in the anesthetized patients studied was of moderate intensity, its incidence

Table 3. Frequency and Severity of Tracheal Lesions Assessed by Endoscopy after Retrieval of the Endotracheal Tube

	Tracheal Mucosal Lesion Score*		
Group	0	1	2
Saline (n = 24)	17 (68)	7 (28)	1 (4)
Air (n = 26)	0 (0)	13 (52)	12 (48)

Values are n (%).

* 0 = no lesions; 1 = one mucosal ulceration; 2 = several mucosal ulcerations.

Table 4. Association between Sore Throat and Tracheal Lesions

	Tracheal Mucosal Lesion Score*		
	0	1	2
Patients with sore throat the day of surgery	3	13	8
Patients without sore throat the day of surgery†	14	7	5

Values are n.

* 0 = normal; 1 = one mucosal ulceration; 2 = several mucosal ulcerations.
† $P < 0.05$ versus patients with sore throat.

should be minimized by monitoring cuff pressure throughout the anesthetic course.

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