Anesthesiology 2001; 95:1125–32

Pharyngeal Function and Airway Protection During Subhypnotic Concentrations of Propofol, Isoflurane, and Sevoflurane

Volunteers Examined by Pharyngeal Videoradiography and Simultaneous Manometry

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Background: **Anesthetic agents alter pharyngeal function with risk of impaired airway protection and aspiration. This study was performed to evaluate pharyngeal function during subhypnotic concentrations of propofol, isoflurane, and sevoflurane and to compare the drugs for possible differences in this respect.**

Methods: **Forty-five healthy volunteers were randomized to receive propofol, isoflurane, or sevoflurane. During series of liquid contrast bolus swallowing, fluoroscopy and simultaneous solid state videomanometry was used to study the incidence of pharyngeal dysfunction, the initiation of swallowing, and the bolus transit time. Pressure changes were recorded at the back of the tongue, the pharyngeal constrictor muscles, and the upper esophageal sphincter. After control recordings, the anesthetic was delivered, and measurements were made at 0.50 and 0.25 predicted blood propotol concentration ($Cp50_{asleep}$) for propofol and 0.50 and 0.25 minimum alveolar concentration ($MAC)_{awake}$ for the inhalational agents. Final recordings were made 20 min after the end of anesthetic delivery.**

Results: **All anesthetics caused an increased incidence of pharyngeal dysfunction with laryngeal bolus penetration. Propofol increased the incidence from 8 to 58%, isoflurane from 4 to 36%, and sevoflurane from 6 to 35%. Propofol in 0.50 and 0.25 $Cp50_{asleep}$ had the most extensive effect on the pharyngeal contraction patterns ($P < 0.05$). The upper esophageal sphincter resting tone was markedly reduced from 83 ± 36 to 39 ± 19 mmHg by propofol ($P < 0.001$), which differed from isoflurane ($P = 0.03$). Sevoflurane also reduced the upper esophageal sphincter resting tone from 65 ± 16 to 45 ± 18 mmHg at 0.50 MAC_{awake} ($P = 0.008$). All agents caused a reduced upper esophageal sphincter peak contraction amplitude ($P < 0.05$), and the reduction was greatest in the propofol group ($P = 0.002$).**

Conclusion: **Subhypnotic concentrations of propofol, isoflurane, and sevoflurane cause an increased incidence of pharyngeal dysfunction with penetration of bolus to the larynx. The effect on the pharyngeal contraction pattern was most pronounced in the propofol group, with markedly reduced contraction forces.**

NORMAL pharyngeal function and airway control is vital for patient safety and comfort after all anesthetic procedures. Although a large number of studies have been performed concerning recovery from anesthesia, few studies have been conducted to determine the return of pharyngeal function and airway protection. Electromyography and latency time to initiate swallowing[1,2] have been used to evaluate the pharyngeal function after propofol and midazolam–propofol administration. This method does not make a more comprehensive evaluation of pharyngeal function possible, nor evaluation of the incidence of aspiration or misdirected swallows. Simultaneous videomanometry may provide detailed information of swallowing patterns and detect dysfunction at various levels in the pharynx.[3] The method has previously been used to study normal swallowing patterns,[3] to examine patients with a history of dysphagia of different origin,[4–6] and to evaluate pharyngeal function during partial neuromuscular block.[7,8]

The current study was performed to evaluate pharyngeal function during subhypnotic concentrations of propofol, isoflurane, and sevoflurane and to compare the drugs for possible differences in this respect.

Materials and Methods

The study protocol was approved by the Local Ethical Committee of Human Research at Karolinska Hospital and Institute (Stockholm, Sweden). Forty-five healthy volunteers (21 men and 24 women) aged 22–41 yr were included after informed consent was obtained. None of the volunteers had undergone surgery of the pharynx, esophagus, or upper airway. They had no history of dysphagia or gastroesophageal reflux and were not taking any medication. Volunteers were randomized into three groups, seven men and eight women in each group, to receive propofol, isoflurane, or sevoflurane.

All volunteers were examined after 4 h of fasting. After arrival in the laboratory, an intravenous cannula was placed in a cubital vein, and a continuous infusion of normal saline was administered at a rate of

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Received from the Department of Anesthesiology and Intensive Care, Karolinska Hospital and Institute, Stockholm, Sweden. Submitted for publication November 29, 2000. Accepted for publication May 30, 2001. Supported by grant No. K2000-04x-13405-014 from the Medical Research Council, Stockholm, Sweden, the Swedish Society of Medicine, Stockholm, Sweden, and AGA Research Funds, Stockholm, Sweden. Presented at the annual meeting of the American Society of Anesthesiologists, Dallas, Texas, October 10–12, 1999.

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100–200 ml/h. The 15 volunteers randomized to receive propofol were provided with two intravenous cannulas, one in the left arm for administration of propofol, and one in the right arm for obtaining blood samples. A manometry catheter was introduced through one nostril and brought forward so as to place the most distal pressure transducer in the upper esophageal sphincter (UES). An anesthesia facemask was placed over the nose and mouth and connected to a breathing circuit, where a mixture of oxygen and air (fraction of inspired oxygen = 0.30) was delivered at 12 l/min. The anesthesia facemask was tailored for this study and provided with sealed passages for the manometry catheter and a separate catheter for administration of contrast medium. In addition, the volunteers randomized to receive propofol were examined with the anesthesia facemask assembled. The study was performed with the subjects in the right lateral position on a radiography table with a 15° head-up tilt. Peripheral arterial oxygen saturation, standard routine electrocardiographic data, and systemic blood pressure were monitored, as well as inspiratory and expiratory oxygen, carbon dioxide, anesthetic agent (end tidal, percent), and respiratory rate (breath/min).

Recordings were made during swallowing of a series of five 10-ml contrast medium (Omnipaque 240 mg/ml, Nycomed, Oslo, Norway) bolus doses. The series of five swallows was repeated at four separate occasions: an initial control recording, two recordings during subhypnotic concentrations of the anesthetic agent, and one recording 20 min after terminating the administration of anesthetic agent. The catheter for administration of contrast medium was placed with the tip in the anterior part of the mouth as felt comfortable for the volunteer. The subjects were asked to form a bolus of the contrast and to swallow when they felt comfortable to do so.

To interpret the degree of sedation experienced by the volunteers, they were all asked to describe their subjective sense of sedation on a visual analogue scale (VAS) before and after the five swallows in each series. The VAS was explained to the volunteers as a scale where 10.0 represents the state of complete wakefulness and 0.0 represents sleep.

Videomanometry

A manometry catheter with four solid-state pressure transducers separated 2 cm apart was used (Konigsberg Instruments, Pasadena, CA). The two distal sensors recorded pressure changes circumferentially, whereas the two proximal sensors recorded pressure in a 180° angle. Correct catheter position was achieved and subsequently confirmed using intermittent fluoroscopy. The most distal pressure transducer was placed in the UES, making the next sensor register pressure changes at the inferior pharyngeal constrictor muscle (PHCI) and the most proximal at the back of the tongue.

The fluoroscopic field covered a lateral projection of the oral cavity, soft palate, laryngeal inlet, and pharyngoesophageal segment. The manometric and fluoroscopic recordings were simultaneously transferred onto videotape for offline analysis.

Analysis of the recorded radiography and manometry was performed as described previously.[7,8] Each contrast bolus swallow was evaluated radiographically for three types of pharyngeal dysfunction, defined as follows: (1) inability to retain the bolus of contrast in the mouth, *i.e.*, premature leakage of contrast medium into the pharynx; (2) misdirected swallowing, *i.e.*, penetration of contrast medium to the laryngeal vestibule; or (3) retention of contrast medium in the pharynx after completion of the swallowing act.

The initiation of the pharyngeal stage of swallowing was evaluated as the time interval between when the head of the bolus passed the anterior faucial arches until the hyoid bone started to move forward (initiation, milliseconds). The transportation (bolus transit time, milliseconds), *i.e.*, the time interval from when the bolus head passed the anterior faucial arches until the bolus tail and the constrictor wave reached the UES, was also measured.

All manometric measurements were calculated as the mean of the five consecutive swallows, except for the UES resting tone. The UES resting tone (millimeters of mercury) was measured before the five swallows. Pressure recordings made at the level of the PHCI and at the back of the tongue were analyzed for contraction peak amplitude (millimeters of mercury), slope of contraction curve (millimeters of mercury per second), and duration of contraction (milliseconds). Coordination between the PHCI and the UES was measured as the time interval between the start of contraction of the PHCI and the start of relaxation of the UES (milliseconds). As the UES is supposed to relax before the contraction of the PHCI, this is a negative value.

Administration of Anesthetic Agents

The 15 volunteers who were randomized to receive propofol had the drug administered by a target controlled infusion pump (Master TCI, Vial Medical, Brézins, France; Diprifusor, AstraZeneca, Cheshire, United Kingdom). After control recordings, the target value was set to 0.50 predicted blood propotol concentration ($Cp50_{asleep}$) (1.8 μg/ml).[9] Recordings were made 15 min after the target value was reached, which was approximately 30 min after start of infusion. The target value was then adjusted to 0.25 $Cp50_{asleep}$ (0.9 μg/ml), and recordings were made when target was achieved. The infusion was then stopped, and final recordings were made 20 min thereafter. Venous blood samples for analysis of actual propofol concentration were taken before the series of five swallows at all test occasions (table 1).

For volunteers who were randomized to receive either

Table 1. Propofol Blood Concentration Verified by Venous Blood Samples before Each Series of Five Swallows

Target Concentration	Blood Concentration (Laboratory Verified)
1.8 μg/ml (0.50 $Cp50_{asleep}$)	1.75 ± 0.46 μg/ml
0.9 μg/ml (0.25 $Cp50_{asleep}$)	0.89 ± 0.40 μg/ml
	0.59 ± 0.35 μg/ml (20 min after the end of infusion)

Mean ± SD.

isoflurane or sevoflurane, the anesthetic agent was administered *via* a vaporizer. After control recordings of five contrast bolus swallows, the vaporizer was adjusted to an end-tidal steady state concentration of 0.50 minimum alveolar concentration (MAC_{awake}) (end-tidal isoflurane, 0.21%; end-tidal sevoflurane, 0.31%),[10] and another series of five swallows was recorded when steady state was reached. The vaporizer was then adjusted to 0.25 MAC_{awake}, and, when the new steady state was reached, another series of bolus swallows were recorded. The anesthetic agent was then turned off, and final recordings were performed 20 min later.

Actual inspired and expired concentrations of anesthetic agent are reported in table 2.

Statistics

All variables except misdirected swallows were analyzed using analysis of variance for repeated measures, followed by Scheffé test. Data are presented as mean ± SD. The frequency of misdirected swallows was analyzed by the Friedman test, followed by Wilcoxon signed rank test to detect differences between control and 0.25 MAC_{awake} of the volatile anesthetics, and control and 0.25 $Cp50_{asleep}$ of propofol. Differences in misdirected swallows between the three groups of propofol, isoflurane, and sevoflurane was analyzed by the Kruskall-Wallis test. The correlation between sedation estimated by VAS and the frequency of pharyngeal dysfunction was analyzed by the Spearman rank correlation coefficient. P values < 0.05 were considered significant.

Results

The three groups were comparable in age distribution (28 ± 5, 28 ± 5, and 30 ± 6 yr), weight, and height. Six men and six women received propofol, seven men and eight women received isoflurane, and five men and eight women received sevoflurane. A comparison between the fluoroscopic and manometric control recordings revealed no differences between the groups, and we thus consider them comparable.

Table 2. Inspiratory and End-Tidal Concentrations (%) of the Inhalational Anesthetic Agents

	Isoflurane		Sevoflurane	
	Inspiratory %	End-tidal %	Inspiratory %	End-tidal %
0.50 MAC_{awake}	0.31 ± 0.04	0.25 ± 0.02	0.47 ± 0.02	0.41 ± 0.02
0.25 MAC_{awake}	0.14 ± 0.02	0.14 ± 0.02	0.22 ± 0.02	0.22 ± 0.02

Mean ± SD.

Pharyngeal Dysfunction and Airway Protection

The three investigated anesthetic agents induced an increased incidence of pharyngeal dysfunction leading to either inability to retain the bolus of contrast in the mouth with premature leakage of contrast medium into the pharynx, misdirected swallowing, *i.e.*, penetration of contrast medium to the laryngeal vestibule, or retention of contrast medium in the pharynx after completion of the swallowing act.

A total of 172 swallows with pharyngeal dysfunction were recorded, 101 of which showed a dysfunction leading to penetration of bolus to the larynx. Retention of contrast medium in the pharynx was detected in 33 swallows, and premature leakage from the mouth to the pharynx was detected in 52 swallows. There were 17 swallows with a combination of bolus penetration, retention of contrast, or premature leakage of contrast. The number of swallows with pharyngeal dysfunction is presented by group in table 3.

Propofol caused a markedly increased incidence of pharyngeal dysfunction in the investigated subhypnotic concentrations. The incidence increased from 8% during control registrations to 58% at 0.50 $Cp50_{asleep}$ and 28% at 0.25 $Cp50_{asleep}$ ($P < 0.001$). Twenty minutes after terminating the propofol infusion, the incidence of pharyngeal dysfunction had returned to 5% (fig. 1).

The inhalational agents also caused an increased incidence of pharyngeal dysfunction at both 0.50 and 0.25 MAC_{awake}. For isoflurane, the incidence increased from 4% (control) to 36 and 29% at 0.50 and 0.25 MAC_{awake}, respectively ($P < 0.001$). For sevoflurane, the corresponding increase was from 6% to 35 and 29%, respectively ($P < 0.001$; fig. 1). Interestingly, there was a strong correlation between the individually estimated sedation on a VAS and the frequency of pharyngeal dysfunction ($P < 0.001$; fig. 2).

Bolus Transportation and Initiation of Swallowing

The bolus transit time was prolonged by the anesthetics from 737 ± 101 ms (control) to 817 ± 150 and 758 ± 118 ms during the two concentrations of the anesthetic agents and 740 ± 116 ms at registrations 20 min thereafter ($P < 0.001$ *vs.* control). There was no difference between the three anesthetics in their effect on bolus transit time. There was no detectable change in the initiation of the pharyngeal stage of swallowing during the experiment.

Table 3. All Recordings with Pharyngeal Dysfunction Presented Group by Group

	Propofol			Isoflurane			Sevoflurane		
	0.50 $Cp50_{asleep}$	0.25 $Cp50_{asleep}$	20 min	0.50 MAC_{awake}	0.25 MAC_{awake}	20 min	0.50 MAC_{awake}	0.25 MAC_{awake}	20 min
Penetration of bolus to the larynx	16	8	2	15	14	3	15	13	6
Retention of contrast	11	9	—	2	3	2	3	3	—
Premature leakage	13	3	1	15	8	2	6	3	1

In the propofol group, there were five swallows with combined dysfunction of bolus penetration, pharyngeal retention, or premature leakage; in the isoflurane group 10 swallows; in the sevoflurane group two swallows.

Manometry

Subhypnotic concentrations of the anesthetic agents caused a reduction of the UES peak contraction amplitude ($P < 0.001$ *vs.* control), the reduction being greatest in the group receiving propofol ($P < 0.001$, propofol *vs.* isoflurane and sevoflurane). The UES resting tone was reduced by propofol at 0.50 and 0.25 $Cp50_{asleep}$ ($P < 0.001$ *vs.* control) and by sevoflurane at 0.50 MAC_{awake} ($P = 0.008$ *vs.* control). Isoflurane did not change the UES resting tone (table 4).

The PHCI peak contraction amplitude and slope of contraction curve were also reduced by the anesthetic agents in the investigated concentrations ($P < 0.001$ *vs.* control). The reduction was most pronounced in the group receiving propofol ($P < 0.001$ and $P = 0.002$, respectively, propofol *vs.* isoflurane and sevoflurane), where the reduction was significant at both 0.50 and 0.25 $Cp50_{asleep}$ ($P < 0.001$ *vs.* control). Isoflurane reduced the PHCI peak contraction amplitude and slope of contraction curve at 0.50 MAC_{awake} ($P = 0.005$ and 0.001, respectively, *vs.* control) but had no detectable effect at 0.25 MAC_{awake}. Sevoflurane reduced the PHCI slope of contraction curve at 0.50 MAC_{awake} ($P < 0.001$ *vs.* control; table 4).

The measurements made at the back of the tongue were only affected by propofol, which caused a reduced contraction peak amplitude and slope of contraction curve at 0.50 $Cp50_{asleep}$ ($P = 0.001$ and 0.007, respectively, *vs.* control). Measurements of the contraction duration of the PHCI and at the back of the tongue showed a tendency to a reduced contraction time in the propofol group and prolonged contraction times in the groups receiving volatile anesthetics. Coordination measured manometrically was affected by the subhypnotic anesthetic concentrations of the anesthetic agents so that the time interval between the relaxation of the UES and the contraction of the PHCI was slightly prolonged ($P = 0.03$ *vs.* control). However, the change was small, from -350 ± 108 ms during control registrations to -394 ± 113 ms and -362 ± 99 ms during administration of anesthetics in the two concentrations and -361 ± 100 ms at registrations 20 min thereafter. When analyzing by group, the change was too small to be statistically significant. There was no difference between the anesthetics in the effect on manometrically measured coordination.

Visual Analog Scale–Estimated Degree of Sedation

The VAS registrations revealed no differences between the three groups (table 5). During administration of the anesthetic agents, the volunteers were allowed to rest as they pleased. Two volunteers in the propofol group, four in the sevoflurane group, and one in the isoflurane

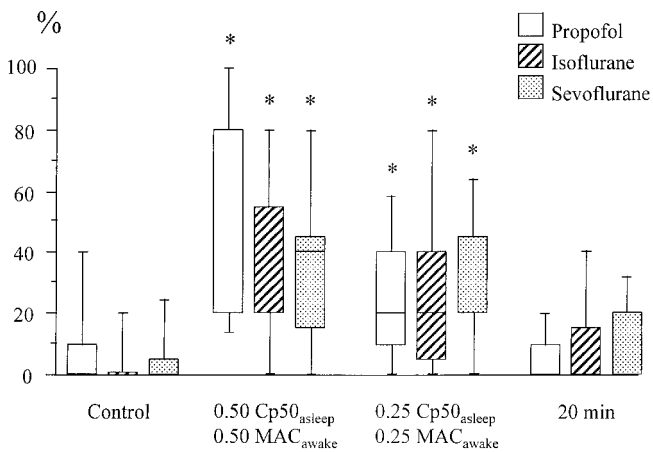

Fig. 1. Frequency of pharyngeal dysfunction (percent) *versus* concentration of anesthetic agent. Box plot displays the 10th, 25th, 75th, and 90th percentiles. *$P < 0.001$ *versus* control.

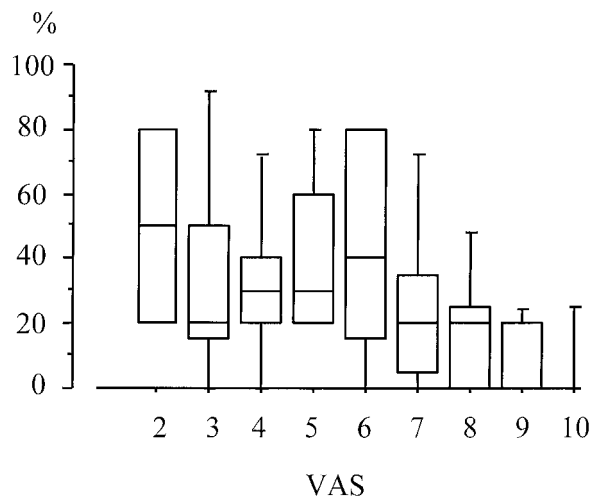

Fig. 2. Frequency of pharyngeal dysfunction (percent) *versus* degree of sedation estimated by the volunteer on the visual analogue scale (VAS; 10 = fully awake, 0 = sleep). Data from all volunteers are pooled together. Box plot displays the 10th, 25th, 50th, 75th, and 90th percentiles.

Table 4. Data for Manometric and Fluoroscopic Variables Presented Group by Group

	Propofol	Isoflurane	Sevoflurane
UES resting tension (mmHg)			
Control	83 ± 36	72 ± 20	65 ± 16
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	39 ± 19*†	61 ± 26	45 ± 18*
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	51 ± 23*	65 ± 25	59 ± 14
20 min after the end of anesthetic delivery	69 ± 30	64 ± 8	57 ± 17
UES contraction peak amplitude (mmHg)			
Control	265 ± 90	236 ± 47	204 ± 40
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	100 ± 56*‡	170 ± 78*	155 ± 30*
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	151 ± 49*	191 ± 65*	158 ± 31*
20 min after the end of anesthetic delivery	207 ± 71	224 ± 66	198 ± 31
PHCI peak contraction amplitude (mmHg)			
Control	177 ± 42	157 ± 49	163 ± 69
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	68 ± 36*‡	116 ± 37*	143 ± 60
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	125 ± 41*	134 ± 56	145 ± 63
20 min after the end of anesthetic delivery	148 ± 43	143 ± 57	160 ± 65
PHCI slope of contraction curve (mmHg/s)			
Control	1207 ± 461	990 ± 314	1188 ± 514
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	425 ± 310*‡	728 ± 310*	857 ± 355*
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	797 ± 291*	901 ± 372	954 ± 454
20 min after the end of anesthetic delivery	1038 ± 296	988 ± 369	1080 ± 455
PHCI duration of contraction (ms)			
Control	354 ± 54	359 ± 63	347 ± 46
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	320 ± 104	359 ± 60	399 ± 84*
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	342 ± 77	328 ± 81	365 ± 63
20 min after the end of anesthetic delivery	336 ± 74	314 ± 57	342 ± 40
TB peak contraction amplitude (mmHg)			
Control	148 ± 50	159 ± 72	177 ± 83
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	94 ± 35*	153 ± 49	173 ± 74
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	144 ± 63	153 ± 79	162 ± 72
20 min after the end of anesthetic delivery	147 ± 46	144 ± 76	190 ± 100
TB slope of contraction curve (mmHg/s)			
Control	765 ± 391	783 ± 516	795 ± 518
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	458 ± 322*	659 ± 371	753 ± 305
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	727 ± 583	779 ± 690	739 ± 291
20 min after the end of anesthetic delivery	793 ± 527	763 ± 604	964 ± 609
TB duration of contraction (ms)			
Control	539 ± 75	560 ± 117	619 ± 103
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	493 ± 97	619 ± 165	663 ± 114
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	556 ± 99	563 ± 132	622 ± 83
20 min after the end of anesthetic delivery	537 ± 77	521 ± 110	596 ± 99
Coordination, manometrically measured (ms)			
Control	−390 ± 59	−317 ± 119	−352 ± 124
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	−456 ± 87	−383 ± 119	−344 ± 107
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	−377 ± 54	−375 ± 120	−329 ± 106
20 min after the end of anesthetic delivery	−399 ± 80	−352 ± 106	−335 ± 108
Initiation of swallowing, fluoroscopically measured (ms)			
Control	89 ± 84	139 ± 106	79 ± 51
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	126 ± 146	144 ± 118	88 ± 68
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	84 ± 123	110 ± 80	98 ± 47
20 min after the end of anesthetic delivery	93 ± 87	122 ± 82	84 ± 40
Transit time, fluoroscopically measured (ms)			
Control	757 ± 96	721 ± 133	738 ± 57
0.50 $Cp50_{asleep}$/0.50 MAC_{awake}	857 ± 186	800 ± 158	799 ± 101
0.25 $Cp50_{asleep}$/0.25 MAC_{awake}	760 ± 97	737 ± 161	779 ± 72
20 min after the end of anesthetic delivery	715 ± 68	730 ± 168	775 ± 67

* $P < 0.05$, versus control. † $P = 0.02$, propofol versus isoflurane. ‡ $P < 0.005$, propofol versus isoflurane and sevoflurane.

group fell asleep during the time between the series of measurements. They were all readily awake on verbal command and could participate at all levels. If a volunteer fell asleep, he or she was ensured to be in a stable state of consciousness by a few minutes of conversation before the estimation of VAS and the series of swallows.

Exclusions from the Study

Five volunteers (one man and two women in the propofol group and two men in the sevoflurane group) were excluded because of frequent uncontrolled swallows during the control recordings and because they found the study stressful. None of the remaining volun-

Table 5. Degree of Sedation Estimated by the Volunteer on a Visual Analog Scale (VAS)

	Propofol	Isoflurane	Sevoflurane
0.50 $Cp50_{asleep}$ 0.50 MAC_{awake}	4.8 ± 1.6	4.9 ± 1.8	4.9 ± 1.3
0.25 $Cp50_{asleep}$ 0.25 MAC_{awake}	6.1 ± 2.1	6.1 ± 1.9	7.0 ± 1.6
20 min after the end of anesthetic delivery	8.5 ± 1.9	9.3 ± 1.4	9.5 ± 0.5

10.0 was considered complete wakefulness and 0.0 represented sleep. All volunteers considered themselves fully awake (VAS 10.0) during the control registrations. Mean ± SD.

teers reported swallowing difficulties during the control recordings or found the study stressful. A total of 787 swallows were analyzed in the remaining volunteers: 240 in the propofol group, 292 in the isoflurane group, and 255 in the sevoflurane group. We were not able to analyze eight swallows in the isoflurane group and five in the sevoflurane group because of either misplaced manometry catheter or disturbed manometric or videoradiographic recording.

Discussion

The main finding of this study is that propofol, isoflurane, and sevoflurane in subhypnotic concentrations cause an increased incidence of pharyngeal dysfunction with penetration of bolus to the larynx. The effect on the pharyngeal contraction pattern was most pronounced in the propofol group, with markedly reduced contraction forces.

Target Anesthetic Concentration

The current study demonstrates that pharyngeal function is impaired by subhypnotic concentrations of propofol, isoflurane, and sevoflurane, thus rendering the patient at an increased risk for aspiration of pharyngeal content during recovery from anesthesia. On the other hand, it does not determine whether the impaired pharyngeal function was caused by anesthetic effect in the brain, peripheral tissue, or both. Furthermore, we do not know whether a potential central effect was primarily related to the cerebral concentration of anesthetic or level of sedation. If sedation level rather than anesthetic concentration is related to pharyngeal dysfunction, one way to ensure equipotent comparison of the anesthetic agents would be titration to a Bispectral Index endpoint. However, since Glass *et al.*[11] found the relation between probability for unconsciousness and Bispectral Index to be different for isoflurane and propofol, and Iselin-Chaves *et al.*[12] found that patients confined to four of the five score levels in the modified observer's assessment of alertness–sedation scale could display identical Bispectral Index values, we chose to investigate pharyngeal function related to effect site (brain and presumably also pharyngeal) concentration and to assess sedation level by a simple self-estimate (10-degree VAS) at each concentration. However, a steady state concentration created for scientific purposes will only constitute a momentary situation after discontinuing the anesthetic, and the concentration decay will depend on several factors, including drug-specific properties. To provide data for an estimate of the duration of potentially harmful pharyngeal effects, we studied the pharyngeal function at two different effect site concentrations of anesthetics.

According to Chortkoff *et al.*,[13] the concentration allowing for regain of consciousness is similar to that at which anesthetics cause loss of consciousness, provided that sufficient time is allowed for equilibration between blood and effect site concentrations. This view is supported by the fact that different studies have yielded similar results for MAC_{awake} for isoflurane, irrespective of whether this concentration was reached from a higher or lower level.[10,14] Because we were unable to find any study giving data on equilibrated wake-up concentration of propofol, we used previous data on concentrations associated with loss of consciousness, assuming a close relation with the corresponding wake-up effect site concentration as discussed by Chortkoff *et al.*[13] Previous data for $Cp50_{asleep}$ of propofol ranges between 2.69 and 4.4 μg/ml.[13,15] Another three studies provided data between these two extremes: 3.3, 3.4, and 3.6 μg/ml.[9,16,17] This variability may be a result of different definitions of loss of consciousness. In the study by Chortkoff et al.[13] (2.69 μg/ml), understanding auditory information and a subsequent purposeful response was required for the definition of consciousness, whereas less demanding cognitive responses were considered sufficient in the studies finding higher $Cp50_{asleep}$ values. MAC_{awake} values for sevoflurane in different studies show only minor variability, and this is also the case for isoflurane. We chose to use MAC_{awake} data from Katoh *et al.*[10] for isoflurane (0.41 ± 0.02%) and sevoflurane (0.62 ± 0.02%), and data from Vuyk *et al.*[9] for propofol, since this study provided an estimate of $Cp50_{asleep}$ in the middle of the concentration range among studies using the same definition for consciousness as for the inhaled agents.

Interpretation of Manometric Recordings

The use of manometric measurements in interpretation of the pathophysiology behind pharyngeal dysfunction must be approached with caution. It is rather the possibility to detect a pattern of changes that is important than to relate the change in each single variable to a typical dysfunction.

The reduced peak contraction amplitude and slope at the back of the tongue and the PHCI may indicate a reduction in the propelling force during swallowing.

Similarly, the reduction in UES peak contraction amplitude indicates an impaired initial propelling force of the bolus down the esophagus, whereas a reduced UES resting tone would affect the protection against regurgitation. Clearly, the reduction in propelling force impairs pharyngeal clearance of bolus content and predisposes for tracheal penetration.

The manometric evaluation of the coordination showed a slightly increased time between the relaxation of the UES and the contraction of the PHCI as an effect on the typical fixed pattern of swallowing by the anesthetic agents. This could represent a central effect of the anesthetic agents. The prolonged transit time measured fluoroscopically is more likely to be an effect of the reduced propelling forces of the pharyngeal muscles. The slower transportation of the bolus that results predisposes for bolus penetration as the bolus stays longer in the "dangerous zone" in the pharynx.

Importance of the Upper Esophageal Sphincter Resting Tone

In a previous study[8] we suggested that the normalized UES resting tone might be used as a marker of return to normal pharyngeal function after partial neuromuscular block. In that study[8] it was clear that the pharyngeal function did not normalize until the UES had regained its resting tone. It is also known that the UES resting tone decreases during sleep.[18] In the current study, the decrease in the UES resting tone was most pronounced in the group receiving propofol. Moreover, the volunteers in the propofol group had a tendency to a higher incidence of pharyngeal dysfunction than those receiving the volatile anesthetics. However, the relation between return of UES resting tension and normalization of pharyngeal function is not that clear. In the isoflurane group, an increased incidence of pharyngeal dysfunction was detected despite the fact that the UES resting tone did not change significantly during the experiment. Moreover, the absolute value of the UES resting tension shows a large interindividual variability. Hence, in clinical practice, it would be necessary with an individual measurement before induction of anesthesia to be able to accurately evaluate the recovery period. At present, measurement of the UES tone is unlikely to be of practical use in routine anesthesia.

Clinical Implications

Previous investigations have shown that sedation and light anesthesia may depress the swallowing reflex and compromise pharyngeal function with risk of aspiration.[19,20] Pharyngeal function may be impaired also during recovery from anesthesia as shown by Rimaniol *et al.*[1] and D'Honneur *et al.*[2] An increased frequency of pharyngeal dysfunction as shown in the current study is thus not surprising. The current investigation was performed with only one drug administered to each volunteer. It is known that anesthetic agents other than sedatives also impair pharyngeal function. We previously showed pharyngeal dysfunction during various degree of partial neuromuscular block,[7,8] and Berg[21] showed an increased incidence of postoperative pulmonary complications in patients with residual neuromuscular block after administration of pancuronium. Patients usually are exposed to several drugs simultaneously during anesthesia and consequently are at risk of their combined residual effects postoperatively.

None of the volunteers in the current study aspirated contrast medium below the level of the vocal cords. However, each bolus contained only 10 ml of contrast medium, and all volunteers were examined in the right lateral position with a 15° head-up tilt. We believe that the lateral position and the function of the true and false vocal cords[22] makes the influence of gravity inefficient for passive flow of material further down into the trachea.

Finally, it is known that elderly patients have a high incidence of pharyngeal dysfunction. Ekberg *et al.*[23] showed that only 16% of patients older than 72 yr had a normal videoradiographic examination, and 65% had varying degrees of misdirected swallowing. Hence, it is possible that these patients are even more susceptible to impaired pharyngeal function from residual concentrations of anesthetic agents.

In conclusion, subhypnotic concentrations propofol, isoflurane, and sevoflurane cause an increased incidence of pharyngeal dysfunction with penetration of bolus to the larynx. The effect on the pharyngeal contraction pattern was most pronounced in the propofol group, with markedly reduced contraction forces.

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