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Technical Note

The Surface Tension of Tracheobronchial Secretions during General Anesthesia

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Tracheobronchial secretions of 26 patients were obtained before and during inhalation anesthesia for determination of surface activity. The mean minimal surface tension (γ_{min}) of these secretions before anesthesia was 26.5 dynes/cm. Halothane and cyclopropane, which are fat-soluble, elevated γ_{min} significantly ($P < 0.001$). Nitrous oxide, which is fat-insoluble, did not affect γ_{min}. These findings demonstrate that fat-soluble inhalation anesthetics can increase the surface tension of tracheobronchial secretions and suggest that measurement of these secretions may be a simple, clinically applicable means of estimating pulmonary surface tension. (Key words: Surface tension; Pulmonary surfactant; Solubility; Airway secretions.)

MEASUREMENT of the surface-active properties of the alveolar lining of the lung (surfactant) requires either an extract from a lung biopsy or material from lung washings. Neither approach can be applied to standard clinical practice. Measurement of surface tensions of tracheobronchial secretions during general anesthesia is simple, and it avoids the hazard associated with lung washings, *i.e.*, interference with normal pulmonary gas exchange. Although these secretions contain surfactant metabolites [1] which probably possess significant surface activity, their surface tensions have not been measured, and their usefulness in estimating alveolar surface tension is unknown. Thus, changes in these surface tensions during anesthesia and the relationship of these changes to the effects of anesthetics on pulmonary surfactant have not been explored. This study was conducted to determine the surface tensions of tracheobronchial secretions obtained before and during general anesthesia and to evaluate the reproducibility of the measured values.

Methods

Tracheobronchial secretions obtained from 31 randomly-selected patients before and after administration of one of three inhalation anesthetic agents were analyzed for surface activity. Informed consent was obtained from each patient at the time of the preanesthetic visit.

Every patient was A.S.A. Class I or II and was scheduled for an elective orthopedic, gynecologic, or general surgical procedure. Premedication included a barbiturate (1–2 mg/kg) and atropine or scopolamine (0.05–0.1 mg/10 kg), given one and a half hours before operation. The patients breathed oxygen for 5 minutes before induction of anesthesia. Endotracheal intubation was accomplished with the aid of sodium thiopental, 3–5 mg/kg, followed by succinyldicholine, 1.5 mg/kg, iv. After the endotracheal tube had been secured and the cuff inflated, 5 ml of sterile saline solution were instilled through the endotracheal tube, and the patient was ventilated with 100 per cent oxygen for a minute. A sterile #16-Fr. suction catheter was then placed in the endotracheal tube and advanced to the orifices of the main-stem bronchi. The orifices of both bronchi and the trachea were suctioned for 5 seconds. Usually, 0.5 to 1.0 ml of material

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TABLE 1. Changes in Minimal Surface Tensions of Tracheobronchial Secretions of 26 Patients

	Patient's Age (years)	Agent	Duration of Anesthesia (min)	Initial Minimal Surface Tension (dynes/cm)	Final Minimal Surface Tension (dynes/cm)	Change
Group I						
	59	N_2O	199	28	26	−2
	32	N_2O	283	26	23	−3
	52	N_2O	65	29	28	−1
	35	N_2O	165	27	25	−2
	31	N_2O	60	27	24	−3
	65	N_2O	150	28	28	0
	41	N_2O	170	30	27	−3
	63	N_2O	95	26	27	+1
	78	N_2O	92	24	24	0
	58	N_2O	65	27	27	0
	31	N_2O	55	25	25	0
MEAN ±SD	49 ±15		127 ±60	27.2 ± 1.9	25.9 ± 1.6	−1.3 ± 1.2
Group II						
	31	Cyclopropane	137	21	27	+6
	39	Cyclopropane	235	23	33	+10
	12	Cyclopropane	55	28	28	0
	50	Cyclopropane	130	27	27	0
	78	Cyclopropane	118	25	31	+ 6
	53	Cyclopropane	81	25	29	+ 4
	67	Cyclopropane	305	28	30	+ 2
	68	Cyclopropane	55	26	28	+ 2
MEAN ±SD	49 ±20		139 ±76	25.5 ± 2.3	29.1* ± 2.0	3.6 ± 3.2
Group III						
	66	Halothane	105	31	33	+ 2
	49	Halothane	235	23	28	+ 5
	43	Halothane	55	26	29	+ 3
	74	Halothane	65	28	35	+ 7
	75	Halothane	215	27	33	+ 5
	77	Halothane	105	27	31	+ 4
	52	Halothane	50	26	30	+ 4
MEAN ±SD	62 ±16		118 ±84	26.9 ± 2.4	31.3* ± 2.4	4.4 ± 1.5

* $P < 0.001$, paired Student's t test.

was aspirated. These secretions were collected in 2-ml Lukens § specimen collectors. Less than 0.5 ml was obtained from two patients by the initial aspiration; in these cases the process was repeated. Sterile saline solution was added to each Lukens tube to make a total volume of 2 ml and the sample was quickly frozen; it remained frozen until analyzed.

§ Specimen Collector of the Pilling Company, Fort Washington, Pa.

After the sample had been obtained, inhalation anesthesia was started and the surgical procedure was begun. Each patient in Group I received nitrous oxide (60–70 per cent) + oxygen (30–40 per cent) + morphine (10–30 mg, iv) or meperidine (75–350 mg, iv). Each patient in Gorup II received cyclopropane (10–50 per cent) + oxygen (50–90 per cent). Each patient in Group III received halothane (0.5–2.0 per cent) + nitrous oxide (60 per

cent) + oxygen (40 per cent). All patients were mechanically ventilated at rates of 8–14 breaths/min and volumes of 8–14 ml/kg/min, measured by a Wright spirometer incorporated in the circle system. In this manner, Pa_{CO_2} was maintained between 32 and 38 torr, as determined at 30-minute intervals in blood samples taken from the radial artery. Ten anesthesiologists, none of whom had any further connection with the study, provided anesthesia for the 31 patients. During the surgical procedures five of the 31 patients had intratracheal pressures greater than 35 cm H_2O (measured at the endotracheal tube) or blood pressure or pulse rate changes of more than 20 per cent from preoperative values; these patients were not included in the study. As the operation was nearing completion, and before the anesthetic gases were turned off, a second and final sample of tracheobronchial secretions was obtained and frozen as described above.

The samples were analyzed on a standard Kimray ¶ pneumatic surfactometer, initially described by Greenfield and Kimmell.[2] This instrument is basically a modified Langmuir-Wilhelmy balance in which a platinum strip subtends the surface of the sampling fluid. Changes in vertical pull (surface tension) on the platinum strip as the surface area is changed by a moving barrier are measured and recorded by a pneumatic sensor and amplification system.

The frozen samples were allowed to thaw and saline solution was added to each to give a final volume of 50 ml. The solution was mixed with a magnetic stirrer and filtered through cotton gauze into the teflon trough of the surfactometer. After 60 minutes of aging in a glass encasement in order to allow the migration of surface-active materials to the surface, compression and expansion cycles were begun. The surface film of each sample was repeatedly compressed and re-expanded until a stable replication of the hysteresis loop was obtained during a two-hour period. The minimal surface tension (γ_{min}), which is a sensitive index of surface activity in surfactant-containing solutions, was recorded for each sample.

¶ Kimray, Inc., 52 N. W. 42nd St., Oklahoma City, Okla.

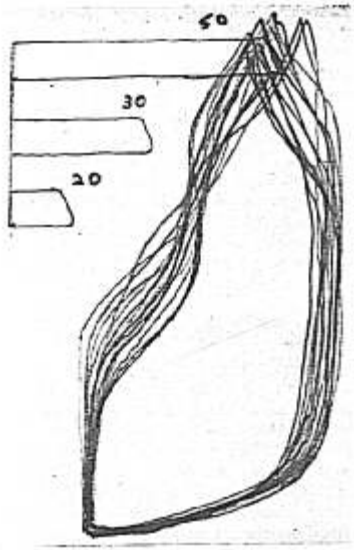

FIG. 1. Hysteresis curves produced by the Kimray surfactometer using a sample of tracheobronchial secretions. Surface area decreases from top to bottom; the values for minimum surface tension are on the left.

Results

Eleven of the 26 patients studied (Group 1) received nitrous oxide supplemented with narcotics, eight (Group II) received cyclopropane and seven (Group III) received halothane (table 1). The three groups were similar with respect to ages of the patients and durations of the operative procedures using the rank and sum test at the 1 per cent level.

The hysteresis curves of tracheobronchial secretions were similar to those obtained with normal lung tissue (fig. 1). Preanesthesia γ_{min} values for all patients ranged from 21 to 31 dynes/cm, the mean being 26.5 dynes/cm. Initial mean γ_{min}'s of Groups I, II, and III were 27.2, 25.5, and 26.9 dynes/cm, respectively. These values were comparable and not significantly different from the mean of the total.

Postanesthetic γ_{min}'s ranged from 23 to 35 dynes/cm, with a mean of 28.2 dynes/cm.

The average increase in γ_{min} of 1.7 dynes/cm in all 26 patients after anesthesia was barely significant ($P < 0.05$), but there was no correlation of duration of exposure to anesthesia with change in surface tension in any group. Final mean γ_{min}'s for the nitrous oxide, cyclopropane, and halothane groups were 25.9, 29.1, and 31.3 dynes/cm, respectively. The increases in γ_{min} of 3.6 and 4.4 dynes/cm after cyclopropane and halothane, respectively, were highly significant ($P < 0.001$) when examined by Student's t test for paired data. The mean decrease of 1.3 dynes/cm with nitrous oxide was not significant.

Discussion

Although it has been shown that anesthetic gases can increase the surface tension of laboratory animals' lungs and model lung systems, these findings have not been confirmed in well-controlled human studies.[3-7] The reason for this is that current methods of obtaining samples of the lung (surfactant) are not readily adaptable to or consistent with safe clinical practice. Lung-tissue extracts must be obtained by thoracotomy, and lung washings are difficult to obtain and frequently increase surface tension in the lungs from which they have been obtained.[8] In an attempt to devise a simple, safe, clinically-applicable measure of pulmonary surface tension, Gluck *et al.*[9] suggested that the surface tensions of secretions of the upper respiratory tract be measured. They theorized that the values obtained would be valid indicators of surfactant activity, because these secretions contain phospholipids similar to those considered to be the alveolar surfactant complex. The results of this study seem to add weight to this suggestion. Tracheobronchial secretions were easily and safely aspirated, they possessed significant surface-tension reducing properties, and γ_{min} values, although higher than those of normal lung extracts (as we expected), were stable, uniform, and reproducible.

Changes were found in the γ_{min}'s of tracheobronchial secretions after halothane and cyclopropane anesthesia, but not after nitrous oxide. The findings with halothane confirm work of Motoyama *et al.*[3] with rabbit lung extracts and Woo *et al.*[4] with excised dog lungs. Clements and Wilson,[5] on the basis of similar results in a model lung system, concluded that all anesthetics alter surface tension, the degrees of change paralleling their solubilities in fat. This conclusion concurs with our results; both halothane and cyclopropane are soluble in fat (fat/blood solubilities of 60 and 14.7, respectively), while nitrous oxide is insoluble in fat (fat/blood solubility 2.3).[10] Other factors, however, must also be considered. Inhibition, reabsorption, dilution, and metabolism of the surface-active material as it moves out of pulmonary alveoli have been shown to occur in unanesthetized animals.[11-14] These factors probably cause the initial (control) γ_{min} values to be in the range of 20 to 30 dynes/cm rather than in the range of 5 to 10 dynes/cm normally found for lung washings or extracts. Anesthetics are known sialagogues,[11] and also inhibit the mucociliary transport system of the lung.[15-17] By these actions they may enhance tracheobronchial inhibition, reabsorption, dilution, or metabolism, as well as delay surfactant migration to the more proximal airways. There is no evidence, however, that halothane and cyclopropane are better secretion stimulators or more effective ciliary inhibitors than nitrous oxide supplemented with opiates. This, the similarity of the initial γ_{min}'s in the three groups, the lack of correlation of duration of exposure to anesthesia with change in surface tension in any group, and the fat solubilities of halothane and cyclopropane suggest that the elevations of γ_{min} of secretions after anesthesia with these two anesthetics are the result of their effects on the surface-active material found in tracheobronchial aspirates.

We cannot conclude, on the basis of these experiments, that the surface tensions of tracheobronchial secretions reflect alveolar surfactant activity, nor can we assume that fat-soluble anesthetics reduce alveolar activity. Even if they did, the changes produced probably would not be clinically significant in the normal individual. Obviously, further work should be done with simultaneous measurements of surface tensions and phospholipids in tissue extracts and upper-respiratory-tract secretions with and without anesthetics. If the results of such studies support and extend the results of the present study, measurement of surface tensions of airway secretions may be-

come an important clinical tool for the assessment of pulmonary surfactant.

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Drugs and Their Actions

METHADONE MAINTENANCE IN SURGICAL PATIENTS Eleven heroin addicts on methadone maintenance (50–120 mg daily) underwent elective surgical operations under general anesthesia. Six with minor surgical problems, such as dental extractions, were continued on their methadone doses without interruption. Postoperative pain was not great and was well controlled by conventional doses of potent analgesics. Five patients underwent major surgical operations such as thoracotomy. Since severe and possibly protracted postoperative pain was anticipated in this group, the daily methadone dose was tapered to 40 mg daily before operation to reduce tolerance to the analgesic effects of other potent narcotics. Conventional doses of meperidine were given for postoperative pain. Methadone was resumed on the second or third postoperative day. In only two of the five patients was postoperative pain well controlled by the regimen. (*Cashman, P. Jr.: Methadone Maintenance Therapy for Heroin Addiction. Some Surgical Considerations, Am. J. Surg. 123: 267–270, 1972.*) ABSTRACTER'S COMMENT: This may be the first published report of surgical procedures in patients maintained on methadone. The author does not particularly recommend methadone withdrawal before operation. Unfortunately, he failed to report details of the anesthetic management. Evaluation of pain and the response to narcotics or analgesics in the postoperative period is probably a complex problem.