Effects of a synthetic lung surfactant on pharyngeal patency in awake human subjects

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Van der Touw, T., A. B. H. Crawford, and J. R. Wheatley. Effects of a synthetic lung surfactant on pharyngeal patency in awake human subjects. J. Appl. Physiol. 82(1): 78–85, 1997.—We examined the effects of separate applications of saline and a synthetic lung surfactant preparation (Surf; Exosurf Neonatal) into the supraglottic airway (SA) on the anteroposterior pharyngeal diameter (Dap) and the airway pressures required to close (Pc) and reopen (Pop) the SA in five awake normal supine subjects. Dap, Pc, and Pop were determined during lateral X-ray fluoroscopy and voluntary glottic closure when pressure applied to the SA lumen was decreased from 0 to −20 cmH2O and then increased to +20 cmH2O. After Surf application and relative to control, Dap was larger for most of the applied pressures, Pc decreased (−12.3 ± 1.9 to −18.7 ± 0.9 cmH2O; P < 0.01), Pop decreased (13.4 ± 1.9 to −6.0 ± 3.4 cmH2O; P < 0.01), and genioglossus electromyographic activity did not change (P > 0.05). Saline had no effect. These observations suggest that pharyngeal intraluminal surface properties are important in maintaining pharyngeal patency. We propose that surfactants enhance pharyngeal patency by reducing surface tension and adhesive forces acting on intraluminal SA surfaces.

upper airway physiology; dosing pressure; opening pressure; surface forces

TWO ANIMAL STUDIES have reported reductions in upper airway resistance and snoring after application of surfactants (surface-active agents that reduce surface tension) into the oropharynx of anesthetized dogs (15, 28). In addition, the application of surfactant to the upper airway can facilitate reopening of the occluded upper airway in dogs (15). Little is known concerning the effects of surfactants on upper airway patency in humans, although Hoffstein and co-workers (11) reported reductions in both the incidence and maximum sound level of snoring in sleeping human subjects after applying a surfactant into the upper airway.

The mechanism by which surfactants may increase upper airway patency is unknown. Widdicombe and Davies (28) reported increased genioglossus muscle electromyographic activity (EMGgg) after applying a mixture of surfactants into the oropharynx of anesthetized dogs. This suggests that surfactants may influence the upper airway by increasing upper airway muscle activity. However, an artificial lung surfactant preparation has been shown to improve upper airway patency in anesthetized dogs with bilaterally sectioned hypoglossal nerves (15). Therefore, factors other than upper airway muscle recruitment may be involved in the improvement in upper airway patency after topical surfactant application.

In a recent study (27), we demonstrated apparent occlusion of the oropharyngeal airway in awake normal subjects when negative pressure was applied to the upper airway lumen via a mouthpiece while the subject voluntarily maintained a closed glottis. Furthermore, the oropharynx still appeared occluded when airway pressure had returned to atmospheric pressure after the applied negative pressure was removed, suggesting that intraluminal surface forces were involved in maintaining apposition of the airway walls. In addition, reopening of the closed oropharyngeal airway only occurred after activation of upper airway-dilating forces during an active inspiratory effort. Therefore, mucosal surface properties of the upper airway may be important in the development and/or maintenance of airway occlusion during periods of negative intraluminal pressure. This suggests that surface tension and adhesive forces in the upper airway may be relevant to the pathogenesis of the obstructive sleep apnoea (OSA) syndrome.

On the basis of these data, we hypothesized that the application of surfactant into the supraglottic airway (SA) would facilitate spontaneous reopening of the occluded oropharyngeal airway in awake normal subjects. Therefore, we examined the patency of the SA during exposure to negative and positive intraluminal pressures both before and after the application of a synthetic lung surfactant preparation into the SA of normal subjects. In addition, the studies were repeated while we measured the EMGgg to examine the effect of the surfactant application on upper airway dilator muscle activity.

METHODS

We measured anteroposterior (A-P) intraluminal SA diameters from X-ray fluoroscopic images in five awake supine male subjects [age 36 ± 1 (SE) yr; body weight 73 ± 7 kg] without a clinical history of sleep disturbance. During voluntary glottic closure, negative and positive pressures were applied to the SA lumen before and after separate applications of saline and a synthetic lung surfactant preparation into the SA. On a separate day, the protocol was repeated in four of the subjects while EMGgg activity was measured without using X-ray fluoroscopy. The protocol was approved by the Westmead Hospital Human Ethics and Radiation Safety Committees, and all subjects gave their informed consent.

X-ray fluoroscopy. The entire SA was viewed by lateral X-ray fluoroscopy by using a mobile X-ray C-arm image intensifier (Phillips BV 25). A 1.0-mm-thick copper filter was used to reduce the dose of radiation received at the skin and to improve the resolution of the air-contrast image. No contrast medium was used. The total thyroid radiation dose in each subject was measured by thermoluminescent dosimetry with the use of lithium fluoride chips and did not exceed 1.6 mGy.
During X-ray screening, negative and positive pressures from a pressure source were applied to the SA lumen during voluntary glottic closure at end expiration (27). During the maneuver, there was no flow through the glottis, and the subjects were instructed to cease respiratory efforts. In four subjects, pressures were applied via a mouthpiece with a nosedip in situ. In the remaining subject, pressure was applied via a modified nasal continuous positive-airway-pressure mask with the mouth closed. During each maneuver, a ramp of negative pressure to $-20$ cmH$_2$O was applied to the SA lumen, followed by a gradual return to 0 cmH$_2$O and then a ramp of positive pressure to $+20$ cmH$_2$O, all for a total time of 20 s. The maneuver was repeated two to three times under each of the following experimental conditions: 1) before application of saline or surfactant into the SA (control); 2) within 3 min after application of 5 ml of hypotonic saline (0.55%, wt/vol) into the SA; and 3) within 3 min after application of 5 ml of a synthetic lung surfactant (Exosurf Neonatal, Burroughs Wellcome Australia; each 5 ml containing 67.5 mg dipalmitoylphosphatidylcholine, 7.5 mg hexadecanol, 5.0 mg tyloxapol, and 29.2 mg NaCl) into the SA. The order of the experimental conditions remained constant, with control runs followed by saline and then surfactant. For each application, 1 ml of saline or surfactant was applied via each nostril and sniffed, and a further 3 ml were applied orally and gargled. The hypotonic saline was intentionally prepared to have the same osmolality as the reconstituted Exosurf surfactant preparation (190 mosmol/l).

The subject's head and neck were immobilized by the mouthpiece or nasal mask and by the X-ray table, to which was attached a pair of head callipers that were applied to the subject's temples. Pressure at the mouthpiece or nasal mask was measured with a differential pressure transducer (CeleSCO, $\pm 100$ cmH$_2$O). Airflow was measured with a pneumotachograph (Fleisch no. 2) coupled to a differential pressure transducer (CeleSCO, $\pm 10$ cmH$_2$O) to determine whether the glottis remained closed while pressure was applied to the SA. The pressure and airflow signals were displayed on an oscilloscope (Fig. 1). The oscilloscope signals were recorded by using a television camera, the electrical output of which was mixed with those from the image intensifier and a digital timer. The mixed signals were displayed on a television monitor and stored on videotape for subsequent analysis (Fig. 1).

EMG. EMG$_{gg}$ activity was measured on a separate day in four of the five subjects by using bipolar Teflon-coated fine-wire electrodes (40 gauge) inserted orally into the body of the genioglossus muscle by using a 23-gauge hypodermic needle (20, 29), with a grounding surface electrode placed on the forehead. The raw EMG$_{gg}$ signal was displayed on an oscilloscope and monitored throughout the study. The raw EMG$_{gg}$ signal was band-pass filtered (100–1,000 Hz), amplified, rectified, and passed through a leaky integrator (Neotrace NT 1900) with a time constant of 100 ms, to produce a moving time average (MTA) EMG$_{gg}$ signal that was recorded together with mouth pressure and flow on a multichannel strip-chart recorder (Hewlett-Packard 7758B). Electrode placement was considered acceptable only if tongue protrusion resulted in recruitment of raw EMG$_{gg}$ action potentials and increased MTA EMG$_{gg}$ activity.

During EMG studies, subjects were placed supine and breathed via a mouthpiece with a nosedip positioned. Negative and positive pressures were applied to the SA lumen during voluntary glottic closure at end expiration in the same manner as for the fluoroscopy studies. The protocol for the EMG study was identical to that for the fluoroscopy study, except that X-ray screening was not performed.

Data analysis. Pharyngeal A-P diameters were related to mouthpiece or nasal mask pressures by analyzing the simultaneous record of the SA fluoroscopic image and pressure signal. Measurements of pharyngeal diameter were made from a monitor screen with the use of a video analyzer (Colorado Video, model 321) coupled to an analog-to-digital converter (IOtech, ADC 488/16A, Cleveland, OH) and a personal computer (27). Vertical and horizontal displacements of the video analyzer cursors on the monitor screen were calibrated from the recorded fluoroscopic image of a steel-ball marker of known dimensions taped to the subject's skin. The steel ball was placed anteriorly over the laryngeal cartilage in the midsagittal line.

In the four subjects in whom pressure was applied via the mouthpiece, the A-P oropharyngeal diameter was measured from the recorded video image at the level corresponding to the cranial limit of the third cervical vertebra (C$_3$) (Fig. 2). In the subject in whom pressure was applied via a nasal mask, occlusion of the nasopharynx during negative pressure preceded and thereby prevented complete oropharyngeal closure. Consequently, in this subject, the A-P nasopharyngeal

![Fig. 1. Schematic diagram illustrating experimental setup used to monitor and record X-ray fluoroscopic image of supraglottic airway, pressure (P) applied to supraglottic airway, and airflow (V). See text for details.](https://jap.physiology.org/doi/10.1213/01.0b3631823445f205)
diameter was measured at a level 1 cm cranial to the caudal limit of the uvulus. The A-P oropharyngeal diameters from four subjects and the A-P nasopharyngeal diameter from one subject were combined and referred to as \( D_{ap} \). In all subjects, \( D_{ap} \) was measured at pressure intervals of 5 cmH\(_{2}O\) from 0 to \(-20\) cmH\(_{2}O\) and from \(-20\) to \(+20\) cmH\(_{2}O\). \( D_{ap} \) was expressed as a percentage of each subject’s control value at 0 cmH\(_{2}O\) before negative pressure. SA closing and reopening pressures (P\(c_l\) and P\(p_o\), respectively) were determined by visual inspection of the recorded SA image and relating this to the recorded pressure signal. P\(c_l\) was defined as the negative pressure where A-P airway occlusion was first observed fluoroscopically at any point along the breathing route. Similarly, P\(p_o\) was defined as the pressure where the fluoroscopic SA image first appeared patent along the entire breathing route. Measurements of P\(c_l\), P\(p_o\), and \( D_{ap} \) were averaged from two or three X-ray screening runs for each experimental condition.

X-ray screening and EMG runs were not included in the analysis if an inspection of the fluoroscopic images, airflow, or EMG signals revealed swallowing, occlusion of the oral cavity when the tip of the tongue was sucked onto the hard palate, or failure to maintain glottic closure. The MTA EMG data was quantified in arbitrary units above electrical zero. Measurements of MTA EMG activity were made when mouth pressure was 0 (before negative pressure), \(-20\), 0, \(+10\), and \(+20\) cmH\(_{2}O\). The EMG data from repeat runs under the three experimental conditions were averaged for each of the five levels of mouth pressure in each subject.

All values are expressed as means ± SE. Statistical analysis of the P\(c_l\), P\(p_o\), and \( D_{ap} \) data was performed with one-way analysis of variance and the least significant difference test. Hysteresis of the \( D_{ap} \)-pressure relationship was assessed by comparing \( D_{ap} \) at corresponding negative pressures as the applied pressure decreased from 0 to \(-15\) cmH\(_{2}O\) and increased from \(-15\) to 0 cmH\(_{2}O\) (paired Students t-test). Statistical analysis of MTA EMG data was performed with the Wilcoxon signed-rank test for paired variates. The null hypothesis for all statistical tests was rejected at P < 0.05 (two-tailed test).

**RESULTS**

Initial attempts to apply pressure via a nasal mask were unsuccessful in two of three subjects because of the occlusion of the nasopharynx, which was unrelated to the application of negative pressure. Hence, we used a mouthpiece to apply the pressure in four subjects. The nasopharyngeal pressure-diameter relationship and the P\(c_l\) and P\(p_o\) data from the remaining nasal mask subject were quantitatively similar to the data from the four subjects in whom pressures were applied via a mouthpiece. Therefore, the results obtained from all five subjects were pooled.

For the mouthpiece-breathing subjects, the airway level of initial occlusion was in the oropharynx, sometimes in association with occlusion of the oral cavity. No hypopharyngeal closure was observed in any subject. For all subjects, the sites of initial occlusion and reopening were not always at the measured D\(ap\) level, so that P\(c_l\) and P\(p_o\) did not necessarily equal the pressures where SA closure and reopening occurred, as measured at the D\(ap\) level.

The effects of saline and surfactant on P\(c_l\) and P\(p_o\) are shown in Figs. 3 and 4. Saline had no consistent effect on P\(c_l\) (control \(-12.3 ± 1.9\) cmH\(_{2}O\), saline \(-11.8 ± 1.3\) cmH\(_{2}O\); P > 0.75), whereas P\(c_l\) was consistently reduced after surfactant (\(-18.7 ± 0.9\) cmH\(_{2}O\); P < 0.01 relative to control and saline). Similarly, saline had no consistent effect on P\(p_o\) (control 13.4 ± 1.9 cmH\(_{2}O\), saline 8.3 ± 3.6 cmH\(_{2}O\); P > 0.25), whereas P\(p_o\) was reduced after surfactant (\(-6.0 ± 3.4\) cmH\(_{2}O\); P < 0.01 relative to control and saline values). Furthermore, positive pressure was not required to reopen the occluded SA in any subject after surfactant (Fig. 4). In contrast, positive pressure was required to reopen the occluded SA in all subjects during control or after saline except in one subject after saline (Fig. 4).

The mean D\(ap\)-pressure relationships before and after applications of saline and surfactant into the SA are shown in Fig. 5. The D\(ap\) progressively narrowed as airway pressure became more negative, and airway closure occurred in all subjects by \(-20\) cmH\(_{2}O\) both before and after saline or surfactant. However, before \(-20\) cmH\(_{2}O\) D\(ap\) was larger after surfactant at \(-15\) cmH\(_{2}O\) relative to control and saline (both P < 0.05).
During control and saline maneuvers, as the pressure was progressively increased from $20 \text{ cmH}_2\text{O}$, the SA generally remained occluded until positive pressure was applied, which resulted in SA reopening. As the positive pressure was increased during control and saline maneuvers, there was progressive SA widening, and $D_{ap}$ at $20 \text{ cmH}_2\text{O}$ did not differ from starting values (at $0 \text{ cmH}_2\text{O}$ before negative pressure). The $D_{ap}$ after saline did not differ from control values at any level of applied pressure (all $P$ values $>0.1$). In contrast, as the pressure was increased from $20$ to $0 \text{ cmH}_2\text{O}$ after surfactant, there was a spontaneous SA reopening in all subjects. After reopening, there was a progressive SA widening as the pressure increased to $+20 \text{ cmH}_2\text{O}$. Hence, $D_{ap}$ after surfactant was larger relative to control at $-15$ (before $-20 \text{ cmH}_2\text{O}$), $-5$, $0$, $+5$, $+10$, and $+15 \text{ cmH}_2\text{O}$ (all $P$ values $<0.05$) and larger relative to saline at $-15$ (before $-20 \text{ cmH}_2\text{O}$), $0$, $+5$ and $+10 \text{ cmH}_2\text{O}$ (all $P$ values $<0.02$).

As demonstrated in Fig. 5, a counterclockwise hysteresis was apparent in the $D_{ap}$-pressure relationship at pressures between 0 and $-20 \text{ cmH}_2\text{O}$. Consequently, $D_{ap}$ during control and saline was significantly larger as pressure decreased from 0 to $-20 \text{ cmH}_2\text{O}$ than at corresponding pressures during the increase from $-20$ to $0 \text{ cmH}_2\text{O}$ ($P < 0.05$ at 0 and $-5 \text{ cmH}_2\text{O}$, respectively). In contrast, after surfactant was applied into the SA, hysteresis appeared diminished (Fig. 5) and did not reach statistical significance at airway pressures between 0 and $-20 \text{ cmH}_2\text{O}$ (all $P$ values $>0.1$).

MTA EMG$gg$ activity did not change after application of saline or surfactant into the SA at any pressure applied to the SA (all $P$ values $>0.05$) (Fig. 6). However, relative to control levels, MTA EMG$gg$ activity tended to be elevated after saline or surfactant at pressures of $+10$ and $+20 \text{ cmH}_2\text{O}$ (Fig. 6).

**DISCUSSION**

The principal finding of this study in awake normal subjects is that the pharyngeal airway is more resistant to collapse and closure from negative intraluminal airway pressure after application of a synthetic lung surfactant and saline.
Surfactant preparation into the SA. Furthermore, reopening of the occluded pharynx is facilitated after surfactant. In contrast, application of saline into the SA lumen had no consistent effect on SA patency, although the SA was subjected to the same maneuvers during the saline runs as during the surfactant runs. Measurements of pharyngeal airway diameter tended to be larger after surfactant, relative to control and saline values, at any given pressure applied to the SA within the −20 to +20 cmH₂O range (except at −20 cmH₂O, where the pharyngeal diameter invariably equaled zero). In contrast, saline had no consistent effect on Pd, Pop, or Dₐp at any of the pressures examined in this study. In addition, saline had no consistent effect on Pd, Pop, or Dₐp at any of the pressures examined in this study.

We previously developed and evaluated an X-ray fluoroscopic method for studying the pressure-diameter relationship of the isolated human SA in the absence of inspiratory effort (27). This method was employed in the present study to determine Pd, Pop, and the pressure-Dₐp relationship. The method provided a lateral view of the entire SA that enabled us to identify the oropharynx and nasopharynx as initial sites of apparent SA closure. One limitation of the technique was the inability to examine changes in the pharyngeal cross-sectional configuration, as our measurements of SA diameter were only made in the A-P dimension. In addition, intrapharyngeal or esophageal catheterization was not performed as an independent means of determining airway closure, because we wished to avoid any possible influence of upper airway catheterization on our results. Therefore, we cannot claim with certainty that 0-mm-diameter A-P measurements during negative airway pressure represent total airway closure.

The retropalatal and oropharyngeal airways lack rigid or bony support and consequently are susceptible to collapse. The collapsible nature of these upper airway segments is clearly evident during obstructive sleep apnea where they are the primary sites of inspiratory narrowing and closure (22, 23). It has been postulated that pharyngeal patency is dependent on the balance between opposing forces generated by the respiratory pump muscles and the upper airway dilator muscles (18). The former promotes upper airway closure during inspiration by generating negative intraluminal pressure, whereas the latter opens or stabilizes the pharyngeal airway. However, the factors that determine pharyngeal patency are not fully understood, and the above model ignores the potential role of intraluminal surface forces.

Clinical lung surfactant preparations such as Exosurf reduce surface tension (5). Our observation that application of Exosurf lung surfactant into the SA can improve SA patency in awake human subjects is, therefore, consistent with a substantial role for intraluminal surface forces in the maintenance of pharyngeal patency when the airway lumen is exposed to modest negative and positive pressures. The findings of this study agree with previous reports of facilitated reopening of the occluded upper airway and reduced upper airway resistance after application of surfactants into the oropharynx of anesthetized dogs (15, 28). In addition, snoring is reduced after application of surfactants into the upper airway of sleeping human subjects (11) and anesthetized dogs (28). This also is consistent with improved upper airway patency after instillation of surfactant into the pharyngeal airway. However, our study is the first to demonstrate that pharyngeal collapse and closure from modest negative intraluminal pressure is attenuated after the application of surfactant into the SA.

The mechanism(s) by which surfactants may promote upper airway patency is not known, and a number of possibilities need to be considered. These include 1) moistening of the upper airway intraluminal surfaces by the liquid surfactant preparation; 2) increased upper airway muscle activity after surfactant; 3) the role of chemical additives in the synthetic lung surfactant preparation; 4) the role of surfactant in reducing surface tension in the upper airway; 5) the role of surfactant in decreasing adhesion between apposed intraluminal surfaces; and 6) the role of surfactant in reducing friction between apposed intraluminal surfaces.

First, moistening of upper airway intraluminal surfaces does not improve SA patency, as application of saline into the upper airway had no consistent effect on upper airway patency. Little is known about the effects of saline and surfactant on the rheological properties of mucus lining the SA. However, the lack of consistent effect of saline on SA patency in this study is consistent with studies in anesthetized animals (15, 28). In addition, it is conceivable that the hypotonicity of the surfactant preparation used in our study may have improved upper airway patency by drawing fluid into the pharyngeal lumen by osmotic. However, this seems unlikely, as the osmolarity of the hypotonic saline used in this study was intentionally matched to that of the synthetic lung surfactant preparation, but the hypotonic saline had no consistent effect on SA patency.

Second, increased EMGg activity has been reported together with reductions in upper airway resistance and snoring after applying surfactants into the oropharynx of anesthetized dogs (28). Because the genioglossus muscle is an important pharyngeal dilator (2, 18), it is feasible that surfactants may improve pharyngeal patency by recruitment of upper airway dilator muscles such as the genioglossus. However, Miki et al. (15) observed facilitated reopening of the occluded upper airway and reduced upper airway resistance after applying an artificial lung surfactant into the oropharynx of anesthetized dogs with bilaterally sectioned hypoglossal nerves. This demonstrates that surfactants can improve upper airway patency in the absence of reflex genioglossus muscle recruitment. In the present study, MTA EMGg activity did not change after application of surfactant into the SA. Although MTA EMGg activity tended to increase after surfactant at +10 and +20 cmH₂O (Fig. 6), this would not have directly influenced the surfactant-related decreases in
Pcl and Pop, as these pressures were invariably subatmospheric after surfactant. Furthermore, the lack of surfactant-related changes in the resting $D_{ap}$ (before application of pressure to the SA) argues against a sustained recruitment of upper airway muscles by surfactant in the absence of significant upper airway pressures.

Although recruitment of raw EMGgg action potentials and increased MTA EMGgg activity consistently occurred in each subject during tongue protrusion, negative airway pressure failed to recruit EMGgg activity in the present study. This differs from findings of other studies that have shown recruitment of EMG activity in the genioglossus and other upper airway muscles during negative airway pressure in awake human subjects and anesthetized animals (12, 14, 25, 26). However, Horner et al. (12) demonstrated substantial intersubject variation in the magnitude of EMGgg recruitment during negative airway pressure, with small levels of recruitment in some human subjects. In addition, in the study by Horner et al., EMGgg recruitment was smaller during voluntary glottic closure than when the glottis was open. Therefore, it is possible that EMGgg recruitment was not observed during negative airway pressure in the present study because EMG measurements were only made in a small number of subjects during voluntary glottic closure. Consequently, we cannot exclude the possibility that Exosurf lung surfactant enhanced SA patency during negative airway pressure as a result of increased recruitment from the genioglossus muscle. In addition, EMG activity was only sampled from the genioglossus muscle, so that involvement of other upper airway muscles cannot be excluded.

Third, the surfactant preparation used in our study contains a number of chemical additives. Exosurf is a synthetic lung surfactant preparation that reduces the severity of respiratory distress syndrome in human infants (1, 3). This synthetic lung surfactant preparation is a mixture of the dominant phospholipid constituent of endogenous pulmonary surfactant (dipalmitylphosphatidylcholine) and the additives hexadecanol and tyloxapol, which have surfactant properties of their own (5) and are believed to enhance dispersion and adsorption of dipalmitylphosphatidylcholine in the lungs. The present study does not enable us to specifically identify which of the constituents of the Exosurf surfactant preparation was responsible for the improved patency of the SA. Nevertheless, the results of this and previous studies (11, 15, 28) have shown that a variety of surfactant preparations with different constituents can improve upper airway patency, suggesting that the surface-active properties of the preparations are primarily responsible.

The role of surface tension forces within the pharyngeal airways has not been investigated. In general terms, the Laplace equation describes the collapsing pressure generated by surface tension within cylinders as being inversely proportional to the internal radius. This suggests that surface tension forces would exert little collapsing pressure within the large pharyngeal airway. However, the pharynx should not be regarded as a simple uniform hollow cylinder. The cross-sectional appearance of the human retroglossal and retropalatal airways is variable and frequently shows marked narrowing in the A-P direction (6, 13, 21, 23). The narrowing is most apparent laterally and frequently gives rise to narrow pleats projecting into the pharyngeal lumen. In awake supine human subjects, the most lateral portions of the pharyngeal pleats may normally be occluded with apparent apposition of the pharyngeal lumen. In awake supine human subjects, the most lateral portions of the pharyngeal pleats may normally be occluded with apparent apposition of the pharyngeal surfaces (13). Theoretically, surface tension forces acting to collapse the pharynx may be substantial at the most lateral patent sections of the narrow pharyngeal pleats where the radius of curvature will be very small. In these regions, pharyngeal collapse may commence in the most lateral patent segment of the pharyngeal pleats and advance medially because of the influence of surface tension forces. In support of this, changes in cross-sectional pharyngeal shape are greater in the lateral than in the A-P direction during nasally applied positive airway pressure (13) and resting tidal breathing (21). We speculate that surface tension forces in the pharyngeal pleats may exert a substantial collapsing force on the pharyngeal walls and contribute significantly to the decrease in the overall cross-sectional area of the pharynx during negative airway pressure. Under these circumstances, a decrease in intrapharyngeal surface tension forces by surfactant may sufficiently attenuate pharyngeal collapse to account for the surfactant-related changes in Pcl and $D_{ap}$ observed in this study. In addition, the radius of curvature of the most lateral patent region of the pharyngeal pleats may decrease as the pharynx collapses, resulting in progressively greater surface tension forces acting on the lateral pharyngeal walls. This could explain why surfactant did not significantly influence $D_{ap}$ until the pharynx had partially collapsed during the application of negative pressure (Fig. 5). Furthermore, the cross-sectional diameter of patent sections of the SA may be very small when the SA begins to reopen, so that a reduction in intraluminal surface tension by surfactant may significantly reduce Pop. Thus decreased surface tension forces in the pharyngeal airway after surfactant may account for the improved pharyngeal patency during negative and positive airway pressures and may play a role in preventing upper airway collapse.

Another potential mechanism of action of surfactants to be considered is that of reducing adhesion between already apposed intraluminal pharyngeal surfaces. Both the present and a previous study from our laboratory (27) have demonstrated that airway pressures less negative than the closing pressure are required to reopen the occluded upper airway. This supports findings from other workers (16, 17, 19, 30) and suggests that apposed intraluminal upper airway surfaces are adherent. Interestingly, both endogenous and exogenous phospholipid surfactants have been shown to reduce adhesion in vitro (4, 7). Furthermore, endogenous surfactants appear to directly bond to the epithelial surfaces of many organs (9, 10, 24), the adsorbed
surfactant lining being likened to a thin polyethylene layer that resists adhesion and makes epithelial surfaces hydrophobic (8, 9, 10). Therefore, we postulate that surfactants applied into the SA are adsorbed to intraluminal SA surfaces and that this may facilitate reopening of the occluded SA by reducing adhesion between apposed intraluminal airway surfaces.

The final mechanism of action of surfactants to be considered is that of lubrication of the intraluminal SA surfaces. Surfactants have long been used as lubricants to reduce friction, and surface-active phospholipids may potentially be highly effective lubricants in vivo (8). It is possible that applied intraluminal pharyngeal surfaces slide over one another during pharyngeal collapse and reopening, with the friction between the sliding surfaces opposing the forces acting to change pharyngeal patency. If surfactant acts to decrease these frictional forces, then this would facilitate both pharyngeal collapse and reopening. However, this is inconsistent with our observation that the pharynx was more resistant to collapse after surfactant was applied into the SA. This suggests that a lubricant action by surfactant is not a major mechanism responsible for increased pharyngeal patency during negative and positive airway pressures after surfactant has been applied into the SA.

Although we cannot exclude a possible contribution from upper airway muscle recruitment, it seems likely from the foregoing discussion that the observed improvements in SA patency after surfactant in our study are predominantly due to reductions in pharyngeal intraluminal surface tension and adhesion, which are effects directly attributable to properties of the surfactant.

Hysteresis was evident in the control $D_{a0}$-pressure relationship (Fig. 5), so that $D_{a0}$ was larger as the applied pressure decreased from 0 to $-20$ cmH$_2$O than at corresponding pressures as pressure increased from $-20$ to 0 cmH$_2$O. This confirms findings from a previous study (27) where we speculated that surface tension may contribute to the hysteresis of the pharyngeal diameter-pressure relationship. Indeed, hysteresis appeared diminished after application of the surfactant preparation into the SA, supporting our view that surfactant lining being likened to a thin polyethylene layer that resists adhesion and makes epithelial surfaces hydrophobic (8, 9, 10). Therefore, we postulate that surfactants applied into the SA are adsorbed to intraluminal SA surfaces and that this may facilitate reopening of the occluded SA by reducing adhesion between apposed intraluminal airway surfaces.

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