Effect of Positive Pressure Ventilation on Surface Tension Properties of Lung Extracts

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The effects of prolonged positive pressure ventilation and overinflation on surface tension properties of the lung were studied in 24 dogs. No alteration of surfactant was observed in 6 animals ventilated at normal pressure and volume for periods up to 6 hours on a Mörch respirator or in 2 nonventilated anesthesia controls. In 10 of 13 dogs subjected to overinflation to a degree sufficient to produce a paradoxical pulse there was absence of surfactant after 24 hours and gross atelectasis. In 3 animals studied immediately after overinflation there was normal surface tension activity. Overinflation of the lung results in depletion or alteration in surfactant which is essential to the maintenance of expanded alveoli at end-expiratory pressures. Prolonged positive pressure ventilation at normal pressure and volume does not alter surfactant and did not result in atelectasis in this study.

Positive pressure ventilation has proved to be a valuable adjunct in the treatment of patients with diffuse atelectasis, severe chest trauma and following open heart surgery. In fact, Damman has advocated the routine use of respiratory assistance in postoperative cardiac patients before signs of respiratory insufficiency are clinically detectable. In our experience, this widespread use of positive pressure respirators has resulted in occasional severe complications including rupture of alveoli with pneumomediastinum or pneumothorax or both. We have also observed respiratory insufficiency during prolonged use of a piston type respirator even though an adequate exchange volume was maintained. In some patients, areas of atelectasis were found at post-mortem examinations. Bronchial plugging by mucus forced peripherally during positive pressure inflation was postulated as one explanation for this atelectasis.

Attention has also been focused recently on the surface active material which lines the alveoli and is essential to the maintenance of expanded alveoli at end-expiratory pressures. The physical concept of surface tension and its application to lung physiology has been reviewed recently by Finley and Clements. The absence or destruction of the surface active agent termed surfactant results in atelectasis. The present experiments were performed on dogs to determine whether positive pressure ventilation and overventilation caused any change in the surface activity of extracts from these lungs.

Methods

Healthy adult mongrel dogs weighing 10 to 15 kg were anesthetized with 30 mg/kg pentobarbital and intubated with a cuffed endotracheal tube. No relaxants were used. Ventilation was performed with a Mörch respirator at a rate of 20/minute with room air at 100 per cent relative humidity and at 27°–30° C. Ventilation pressures were measured directly with a manometer attached to a T-extension from the endotracheal tube. In determining the degree of overinflation, a physiological end point was used by palpating the femoral arterial pulse wave as the inspiratory volume was increased until a detectable paradoxical pulse occurred. Inflation pressures of 26–32 cm. of water usually were required to produce this effect. The respiratory rate was maintained at 20/minute in all experiments. In the control animals, the peak inflation pressures were 6–10 cm. of water with volumes of 14 mL/kg. body weight as an estimated normal tidal exchange.

Following the period of artificial positive pressure ventilation, the animals were allowed to recover and 24 hours later underwent sterile thoracotomy. The lower lobes were
selected for all lung biopsies and often showed areas of gross atelecstasy. In some dogs repeat thoracotomy and rebiopsy of the lower lobes were performed 48 hours following the ventilatory procedure. The lung biopsies weighing 5 g. were frozen immediately and were studied by extraction in 50 ml. saline. Surface tension of the material extracted from the lung biopsies was measured directly on a modified Wilhelmy balance by the method of Brown, Johnson and Clements. The self-cycling balance changed surface area from 55 cm.² to 8,5 cm.² over a 10-minute period. Each sample remained on the balance for a period of 1–3 hours determined by the replication of maximum and minimum readings for several cycles, and the final reading was the lowest minimum value recorded. The minimum surface tension reading was considered to be within the normal range when less than 15 dynes/cm., but the extract stability index representing the change of tension/average tension was also calculated according to the formula:

\[ \delta = \frac{2 \times (\text{max. reading} - \text{min. reading})}{(\text{max. reading} + \text{min. reading})} \]

The values of \( \delta \) were considered normal when they were 1,00 or greater.

Control animals included 2 dogs which were anesthetized and intubated but not placed on a respirator (group A), three dogs which were ventilated at normal pressures for two hours and three dogs which were ventilated at normal pressures for 3–6 hours (group B).

In 3 dogs, measurements of the surface tension of extracts from the lung biopsies were performed immediately following periods of overinflation from 1 1/2–3 1/2 hours (group C). In the remaining 13 days subjected to overinflation, observations were made 24 hours following ventilation for periods of 1–2 hours. In two of these dogs, a Carlens tube was used to allow selective overinflation of one side with the opposite side serving as a control at normal respiratory pressures.

**Results**

The control animals, as shown in figure 1, showed no alteration in surface tension of lung extracts 24 hours after they were ventilated at normal pressures and volumes for periods up to 6 hours (group B). Similarly, there were no alterations in extract surface tension following general anesthesia and intubation without artificial ventilation (group A). The average minimum surface tension and \( \delta \) readings were well within the normal range as shown in table 1.

Group C consisted of three dogs subjected to overinflation for periods of 2–5 hours. Thoracotomies and lung biopsies were performed immediately in these animals which uniformly showed signs of pulmonary edema and right heart failure. Extracts of these lung biopsies were normal in average minimum values and calculated \( \delta \) (table 1). The individual maximum and minimum surface tension readings for each group are shown in figure 1.

In four dogs subjected to 1 hour of overinflation (group D) lung biopsies obtained 24 hours later showed varied effects. The surface tension was high in two dogs and was borderline in another dog, which showed a minimum surface tension of 18 dynes/cm. (fig. 1).
one dog, the surfactant was present and a minimum reading of 5 dynes/cm. was obtained. The $s$ value of 1.05 is borderline but not clearly abnormal.

Seven dogs were studied after 2 hours of overinflation of both lungs (group E). In five of these, diffuse atelectasis was observed at thoracotomy 24 hours later and analysis of lung biopsy material showed minimum surface tension readings between 35–50 dynes/cm. In two of these with atelectasis, a repeat biopsy of the lower lobe 48 hours after overinflation showed return of the normal surface tension effect (minimum values less than 15 dynes/cm.) and disappearance of the atelectasis. In figure 2 tracings of representative surface tension readings show persistently elevated surface tension at 24 hours followed by the appearance of normal low surface tension at 48 hours and at 72 hours in this animal.

**TABLE 1. Average Surface Tension Readings Obtained After Positive Pressure Ventilation at Normal or Elevated Pressures**

<table>
<thead>
<tr>
<th>Group</th>
<th>Dog</th>
<th>Procedure</th>
<th>Time (hours)</th>
<th>Surface Tension (dynes/cm.)</th>
<th>$s$</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Average Maximum</td>
<td>Average Minimum</td>
</tr>
<tr>
<td>A</td>
<td>2</td>
<td>Anesthesia and intubation control</td>
<td>3</td>
<td>38</td>
<td>7</td>
</tr>
<tr>
<td>B</td>
<td>6</td>
<td>Normal ventilation</td>
<td>2–6</td>
<td>38</td>
<td>6</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>Overinflation immediate biopsy</td>
<td>2–5</td>
<td>37</td>
<td>2</td>
</tr>
<tr>
<td>D</td>
<td>4</td>
<td>Overinflation 24-hour biopsy</td>
<td>1</td>
<td>45</td>
<td>14</td>
</tr>
<tr>
<td>E</td>
<td>7</td>
<td>Overinflation 24-hour biopsy</td>
<td>2</td>
<td>40</td>
<td>38</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>48-hour biopsy (2 dogs)</td>
<td></td>
<td>38</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Selective overinflation (left lung, 24-hour biopsy)</td>
<td>2</td>
<td>49</td>
<td>30</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(left lung, 48-hour biopsy)</td>
<td></td>
<td>40</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Normal ventilation (right lung)</td>
<td></td>
<td>37</td>
<td>5</td>
</tr>
</tbody>
</table>

*The average maximum and minimum values are based on one determination in each dog unless specified otherwise.

**FIG. 2.** Tracings made from the records of an animal subjected to two hours of overinflation. After 24 hours the extracts of a lung biopsy shows no change in surface tension during the decrease in surface area. However, at 48 and 72 hours, there is evidence of surfactant material as surface tension falls with decreasing surface area. The arrows indicate the direction of change of surface area.
The remaining two dogs in the group had normal surface tension readings, although there was a diffuse mottling of the lungs noted at thoracotomy. The $s$ value of 0.39 on the average maximum and minimum surface tension readings in the group is clearly abnormal.

To confirm the effect of overinflation, two dogs were intubated with a Carlen's tube and the left lung selectively overinflated while normal pressures were maintained in ventilating the right lung. In both dogs, thoracotomy at 24 hours revealed atelectasis only on the left side. Extracts of lung biopsies from the left side showed an average minimum surface tension of 36 dynes/cm. compared with a minimum of 5 dynes/cm. obtained from extracts of the right lung (fig. 3). Repeat biopsy of the left side in these two dogs in 48 hours showed a return of low surface tension (table 1).

Discussion

The layer of a surface active lipoprotein lining the alveoli serves to equalize pressures between large and small alveoli, and stabilize the alveoli at end-expiratory pressures. The absence of this material has been associated with hyaline membrane disease in infants and the postperfusion lung syndrome. In vitro studies suggest that the alveoli may contain a fixed amount of surface active material without a reserve which can be readily mobilized and that overstretching the layer may destroy the surface properties. In studies of the epithelial lining of the alveoli by electron microscopy, Schulz has shown granular cytoplasmic degeneration and disruption of normal architecture following hyperinflation.

This purely mechanical explanation, however, does not account for the preservation of surfactant observed in the acute studies where lung biopsies were obtained immediately following the period of overinflation. Instead, the delay in appearance of atelectasis suggests that the ability of the alveolar cell to maintain or restore the surface layer may have been impaired. The circulatory changes produced by overinflation include intermittent interruption of pulmonary capillary blood flow at the peak of inflation pressure and, in some animals, pulmonary edema was produced immediately following the ventilatory period. It has been reported that ligature of the main pulmonary artery produces a selective loss of surfactant in the affected lung. However, preliminary studies in this laboratory on dogs show preservation of surface active material for at least 48 hours after unilateral pulmonary artery division. Although pulmonary edema may occur during the brief transition period
when circulatory adjustments are being made after overinflation, the biopsies obtained at this time show normal surface activity. Finally, since larger volumes are necessary to produce the overinflation, there may be a regional effect from altered gas exchange and a lower CO₂ tension. Although these effects have not been dissociated, it seems evident that alveolar lining cells, which are thought to produce surfactant, are susceptible to both the physiological and mechanical alterations produced by overinflation.

This study suggests that over inflation of the lung results in depletion, alteration, or interference with the action of surfactant, whereas prolonged positive pressure ventilation at normal inflation pressures has no deleterious effects on alveolar surface tension. It may be postulated that respiratory insufficiency and atelectasis which have occasionally been observed with a fixed volume piston type respirator may be due in part to depletion of surface active material and not necessarily to plugging of the bronchi. In routine use of positive pressure respirators on patients with normal lungs significant elevation of ventilatory pressure can be avoided by restriction of inflation volume. Maintenance of normal volume and pressure in the respiratory system will prevent overdistension of the lung and, according to our data, may also avoid subsequent alteration of alveolar surface tension.

Summary

The effects of positive pressure ventilation and overinflation on the surface properties of the lung were studied in dogs. Surface activity of extracts was abnormal in 10 out of 13 dogs studied 24 hours after overinflations and was associated with diffuse atelectasis. No alteration in surface tension of lung extracts was observed in dogs ventilated with normal volume and pressure for periods up to 6 hours. The clinical implications and possible mechanisms for the alteration of alveolar surface tension are discussed.

References