Pulmonary Lavage with Liquid Fluorocarbon in a Model of Pulmonary Edema

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An animal model of a specific type of acute pulmonary edema was produced by instilling a concentrated sucrose solution into each mainstem bronchus of 20 dogs. The resulting disease was treated with either 100 per cent oxygen via fixed-volume ventilation with PEEP at 10 cm H2O (control group), or pulmonary lavage with oxygenated Caroxin-D fluorocarbon liquid for one hour followed by reconversion to breathing 100 per cent oxygen by mechanical ventilation with PEEP. More edema fluid was recovered during the washout period (22.5 ± 8 ml/kg) than during the corresponding time in the control group (14.2 ± 10 ml/kg). The washout group also had a significantly higher and more prolonged elevation in PaO2 than the control group. Pulmonary lavage with fluorocarbon in the treatment of acute, massive pulmonary edema appeared beneficial and warrants further study. (Key words: Pulmonary edema; Pulmonary lavage; Fluorocarbon; Liquid ventilation; PEEP; Sucrose.)

Previously, we investigated the effects of ventilation with liquid fluorocarbons on the pulmonary physiology and histology of the dog.‡§ While we have shown that some secretions can be removed during liquid ventilation, the technique has not been applied to animals with severe pulmonary disease to evaluate its therapeutic value. To determine whether simultaneous bilateral pulmonary lavage with fluorocarbon liquid would be beneficial in severe disease states, we designed an experiment to determine whether massive pulmonary edema fluid, produced by aspiration of concentrated sucrose solution, could be washed from the lungs of a dog, thereby resulting in improved arterial oxygenation.

Materials and Methods

Twenty healthy dogs, weighing 10 to 19 kg, were divided into two equal groups. All dogs were anesthetized with sodium pentobarbital, 25 mg/kg, iv, and their tracheas intubated with a cuffed endotracheal tube. A catheter was placed in the femoral artery to record blood pressure and collect blood for determination of gas tensions and pH. Another catheter was positioned in the superior vena cava to record central venous pressure and administer maintenance electrolyte fluids. PaO2, Paco2, and pH2 values of all animals were determined while they breathed air and after they had breathed 100 per cent oxygen for 15 minutes.

Corn syrup," 5 ml/kg, was divided into two equal amounts and injected into each mainstem bronchus via a no. 18 French catheter. All animals breathed oxygen spontaneously for 5 minutes. Then, they were paralyzed with succinylcholine chloride, 0.5 mg/kg, iv, and ventilated with a volume-limited ventilator,** set to deliver 100 per cent oxygen at a tidal volume of 30 ml/kg, for 15 minutes. Minute ventilation was regulated by adjusting the rate to maintain a PaCO2 of approximately 50 mm Hg. In one group ventilation was continued as above for the next three hours, but with the addition of positive end-expired pressure (PEEP) at 10 cm H2O. The other group was ventilated with oxygenated Caroxin-D fluorocarbon liquid,§§ instilled from a reservoir as described previously‡§ at minute volumes of 1,500 to 2,000 ml/min for an hour and drained by gravity. The fluorocarbon was then drained....

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from the lungs and each animal was reconverted to breathing 100 per cent oxygen by constant-volume ventilation with PEEP, as above. Pulmonary edema fluid was collected by gravity drainage during breathing of air and by separation from the fluorocarbon during liquid breathing. The quantity was measured, and the edema fluid lost was replaced with an equal volume of Ringer’s lactate solution via the central venous catheter. The dogs were sacrificed after three hours and their lungs removed for gross and histologic examination.

The lungs and tracheas were removed en bloc and photographed. The right mainstem bronchus was cross-clamped and the right lung fixed by immersion in 10 per cent buffered formalin. The left lung was inflated with 10 per cent buffered formalin at 30–50 cm (formalin) pressure and fixed for two or more days prior to sectioning. Samples for histologic examination were taken from each lobe. All lobes were inspected and any areas that appeared abnormal were included in the samples. An average of 10 sections was taken from each lung; sections were stained with hematoxylin and eosin.

**Results**

Corn syrup instilled into the bronchi produced copious edema fluid within 5 minutes. The amount of edema fluid recovered during fluorocarbon washout, 22.8 ± 8 ml/kg (mean ±SD), was greater than that collected during the corresponding period from the control animals, 14.2 ± 10 ml/kg ($P < 0.07$). However, the total volumes of edema fluid recovered in the three-hour experiment were 46.2 ± 13 ml/kg in the fluorocarbon-washout group and 43.6 ± 9 ml/kg in the control group.

The animals were considered to be normal prior to the experiment when their $P_{a02}$'s were more than 70 torr during breathing of room air and 400 torr during breathing of 100 per cent oxygen. Before instillation of the corn syrup, the room-air $P_{a02}$ in the control group was 92 ± 14 torr (mean ±SD) and that in the fluorocarbon group was 78 ± 4 torr. These values were not significantly different ($P > 0.2$). The $P_{a02}$'s at $F_{O2}$ = 1.0 were 472 ± 32
torr in the control group and 438 ± 29 torr in the fluoro carbon group. Twenty minutes after instillation of corn syrup, the $P_{aO_2}$'s at $F_{O_2} = 1.0$ were 213 ± 128 torr in the control animals and 176 ± 100 torr in the fluoro carbon group. The $P_{aO_2}$ of the control group increased slightly after 15 minutes of PEEP, and then steadily declined in the remaining three hours (fig. 1). The $P_{aO_2}$ of the fluoro carbon group increased significantly following washout when these...
dogs were reconverted to oxygen ventilation with PEEP (385 ± 60 torr). Pao2 peaked after 90 minutes of treatment, then declined, but it remained significantly higher than that in the dogs treated with mechanical ventilation and PEEP only (P < 0.001) (fig. 1).

The Paco2 and pH values of the control dogs remained essentially unchanged, whereas the washout group developed respiratory acidosis during liquid ventilation (P < 0.001) (fig. 2). Pao2 and pH values of this group rapidly returned to normal after reconversion to gas breathing.

Systolic and diastolic blood pressures varied in a cyclic manner during positive-pressure ventilation and fluid ventilation, with the peaks occurring during expiration and valleys during inspiration. The pulse pressure also narrowed. Systolic pressure was restored when Ringer's lactate solution was used to replace the edema fluid lost. Central venous pressure increased approximately 3 to 4 cm H2O during PEEP.

On microscopic examination, all sections showed hyperemia and various degrees of interstitial and intra-alveolar edema. In many sections, polymorphonuclear leukocytes were numerous in the septal capillaries. They were also scattered in the edema fluid and in the lumina of some bronchioles. Hyperemia, edema, and leukocytic infiltrates were present equally in control and experimental groups. No specific reaction to fluorocarbon was seen, as lung tissues from the two groups were indistinguishable histologically.††

**Discussion**

We demonstrated that pulmonary edema fluid and viscous sucrose solution can be washed from the lungs by total-lung lavage with oxygenated Caroxin-D liquid fluorocarbon at 1 atmosphere. Furthermore, there was a significant increase in Pao2 when oxygen was breathed again. The amount of edema fluid recovered from the lungs in one hour of lavage was greater than in the control group. However, the total volumes of edema fluid recovered in the two groups in the three hours were comparable.

The relatively large amount of fluid recovered during the washout period may have been the mechanism for the initial increase in oxygenation. Another mechanism that might have been effective in the improvement in arterial oxygenation found was the displacement of edema fluid in the alveoli by fluorocarbon, which has a higher solubility coefficient for oxygen (42 vol per cent at 37°C at 1 atm) than aqueous fluids. This would preferentially favor the diffusion of oxygen through the fluorocarbon-filled alveoli. Approximately 200 to 400 ml of fluorocarbon cannot be recovered by drainage of the lungs at the conclusion of lavage. A small amount of this is lost as a result of evaporation. The bulk, however, remains in the periphery of the lung.35 The presence of this fluorocarbon in the alveoli also may prevent its collapse, thus acting as a mechanical surfactant.

It is interesting that Pao2 decreased an hour after liquid ventilation was terminated, although it was still significantly higher than that in the control animals. This may have been caused by continuous edema formation. Further experimentation is necessary to determine whether repeated fluorocarbon lavage will be beneficial in removing additional edema fluid and improving oxygenation.

We conclude that massive pulmonary edema fluid caused by aspiration of concentrated sucrose solution can be washed from the lung by lavage with fluorocarbon liquid at 1 atmosphere, with improvement in arterial oxygenation.

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**References**


