

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 (22.8 ± 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 Pa_{o₂} 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.¹⁻⁴ 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. Pa_{o₂}, PaCO₂ and pH_a 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 30 torr. 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.^{2,3} 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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¶ Karo Light Corn Syrup, CPG International, Inc., Englewood Cliffs, N. J.

** Emerson Post Operative Ventilator, J. H. Emerson Co., Cambridge, Mass.

†† Trademark of Allied Chemical Corporation, Morristown, N. J. (previously identified as P-1D).

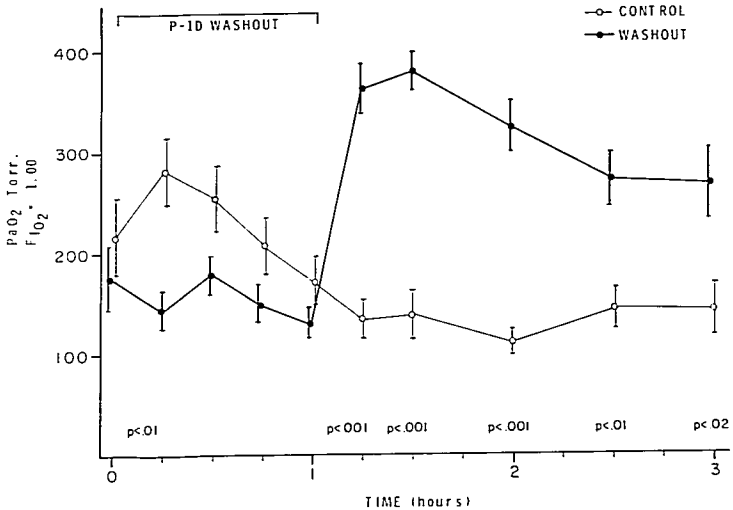


FIG. 1. PaO_2 's (means \pm SEM) during treatment of massive pulmonary edema. "Control" received CPPV; "washout" received bilateral lung lavage with Caroxin-D fluorocarbon liquid followed by CPPV.

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 \pm 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 PaO_2 '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 PaO_2 in the control group was 92 ± 14 torr (mean \pm SD) and that in the fluorocarbon group was 78 ± 4 torr. These values were not significantly different ($P > 0.2$). The PaO_2 's at $\text{FIO}_2 = 1.0$ were 472 ± 32

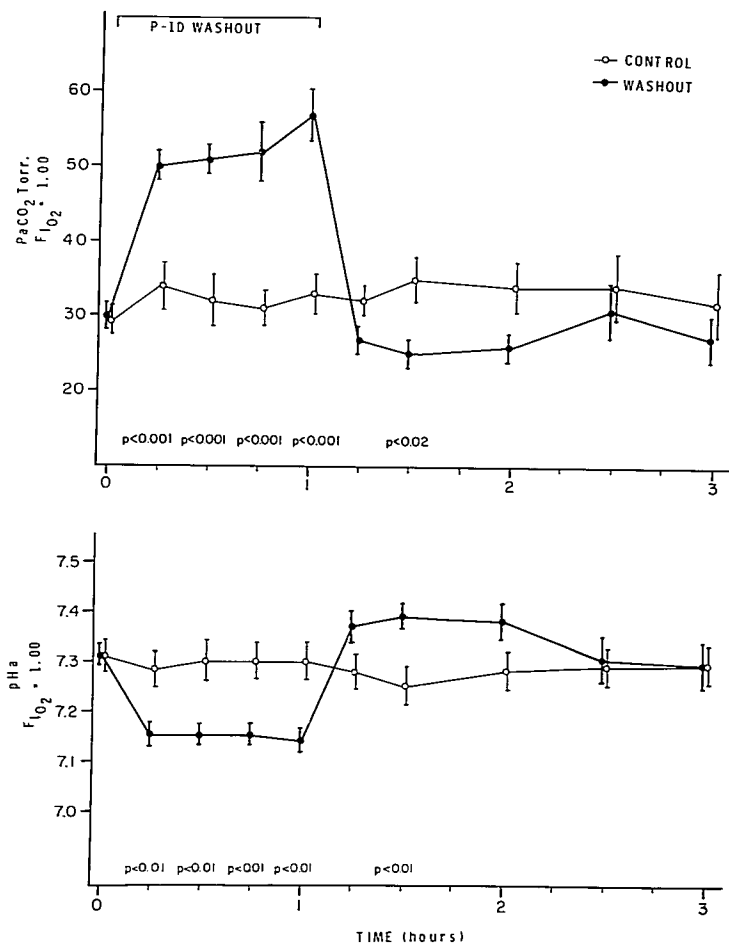


FIG. 2. PaCO₂ and pH_a values (means ± SEM) during treatment of massive pulmonary edema. "Control" received CPPV; "washout" received bilateral lung lavage with Caroxin-D fluorocarbon liquid followed by CPPV.

torr in the control group and 458 ± 29 torr in the fluorocarbon group. Twenty minutes after instillation of corn syrup, the PaO₂'s at F_IO₂ = 1.0 were 213 ± 128 torr in the control animals and 176 ± 100 torr in the fluorocarbon group.

The PaO₂ of the control group increased slightly after 15 minutes of PEEP, and then steadily declined in the remaining three hours (fig. 1). The PaO₂ of the fluorocarbon group increased significantly following washout when these

dogs were reconverted to oxygen ventilation with PEEP (385 ± 60 torr). P_{aO_2} 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 P_{aCO_2} and pH_a values of the control dogs remained essentially unchanged, whereas the washout group developed respiratory acidosis during liquid ventilation ($P < 0.001$) (fig. 2). P_{aCO_2} and pH_a 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 H_2O 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 P_{aO_2} 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

†† Fluorocarbon does not stain with hematoxylin and eosin and drops out during histologic preparation.

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 alveolus. 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.³⁻⁵ The presence of this fluorocarbon in the alveolus also may prevent its collapse, thus acting as a mechanical surfactant.

It is interesting that P_{aO_2} 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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